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Original Articles

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THE EFFECTS OF MERCURY INHALATION UPON THE ANIMAL ORGANISM*

A Pathologic Study

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(Received for publication, September 1, 1922)

THIS paper is an account of observations upon the effects of mercurial vapors on the animal organism. The experiments which it describes were undertaken with the object of discovering the pathologic changes, if any, which occur in the tissues of animals subjected to inhalations of mercurial vapors. These investigations appeared to be much needed at this time—first, because of the nearly total absence of information on the subject; and, second, because of the growing interest among syphilologists in mercurial inhalations as a therapeutic measure in the treatment of syphilis. There are many pathologic reports describing the tissue changes observed in animals subjected to every manner of mercury administration except inhalation; it is also well known what pathologic changes mercurial poisoning produces in the human organism, as occasions for postmortem examinations of suicides and other persons who have succumbed to the effects of mercury compound are frequent. But even the most careful search of the literature fails to reveal any ample description of the gross or histologic changes in organs after death from inhalation, for mercury inhalation deaths are rare, and records of their postmortems are not obtainable. Indeed, there are not many well authenticated cases of death from mercury vapor inhalation on record; and even of the few known, such as those that occurred on the ship Triumph, where many were poisoned and several died from emanations escaping from broken mercury containers in the hold of the vessel, there is lack of autopsy information.

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*From the Experimental Laboratories of the Brooklyn Diagnostic Institute.

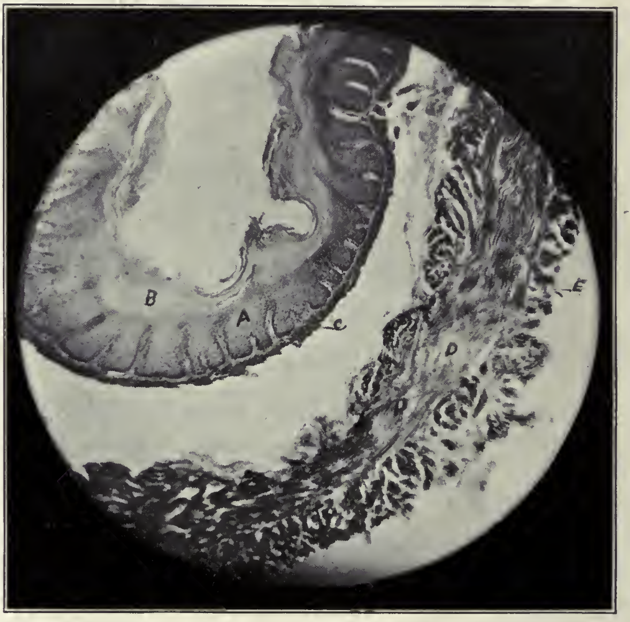

Fig. 1.—Esophagus, low magnification. *A,* stratified epithelial layer of mucosa with indefinite outline and cloudiness of its cells, covered by a mass of hyaline substance *B. C,* muscularis, separated at some points from the underlying and markedly edematous submucosa. *D,* circular muscular coat with bundles separated by edema, which also invades the longitudinal fibers, *E.*

The mercurial vapor therapy of syphilis, after having been used for centuries with an enthusiasm almost extreme, fell for a long time into discredit that was almost universal and also extreme.

Fumigations were reproached with being not only unpleasant but dangerous. It is true that they did at times have disastrous consequences; the defects, however, were not always inherent in the vapors themselves but in the methods of their administration. There appears to be now a revival of interest in this mode of treating syphilis, perhaps because of the recent movement to establish the simplest, safest, most pleasant, least harmful and most active means of treating this disease. The manner of employing mercury is still a problem; the mercurials in use at present and the methods of their administration have not met all the required demands. Hence, attention is again directed to inhalations. This is shown of late by the increased number of published scientific studies on the subject, and especially by the wider application of mercury vapor therapy in institutions and in private practice. This renewed interest and the lack of pathologic information furnished the stimulus for these investigations and for other work to be reported shortly.

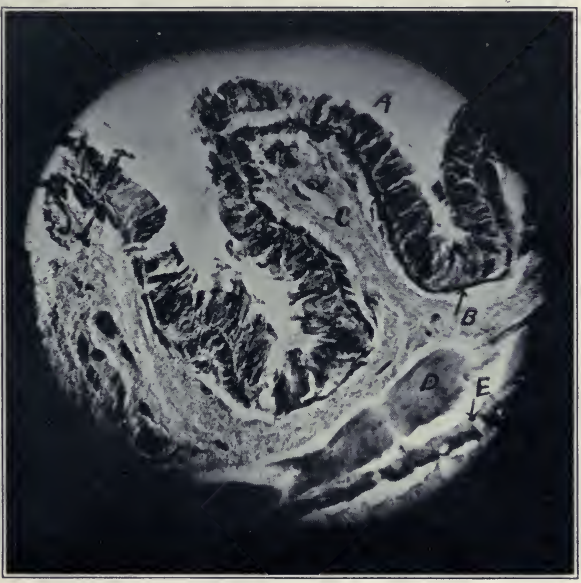

Fig. 2.—Small intestine, low power. Guinea pig, Experiment 5, showing intestinal villi with considerable destruction of the epithelial layer, *A*, shedding of individual cells and of whole portions of the mucosa. The submucous layer, *C*, is edematous and in places separated from the muscular is mucosa, *B*. The edema also involves the muscle bundles of the external coat, *D* and *E*.

EXPERIMENTS

The experiments, with but few exceptions, were conducted on guinea pigs. In the beginning rabbits were also used, but these were soon abandoned because, first, guinea pigs are smaller and more easily handled; second, they are apparently more susceptible to pathologic affections of man than are rabbits; third, the smaller organs of guinea pigs were more convenient for chemical analysis, as it was designed to use the whole and not a portion of the organ in the detection of mercury and its quantitative estimation; fourth, because the chemical and pathologic findings in our early comparative experiments upon the two species were identical, and it was consequently thought permissible to confine ourselves to experiments on guinea pigs.

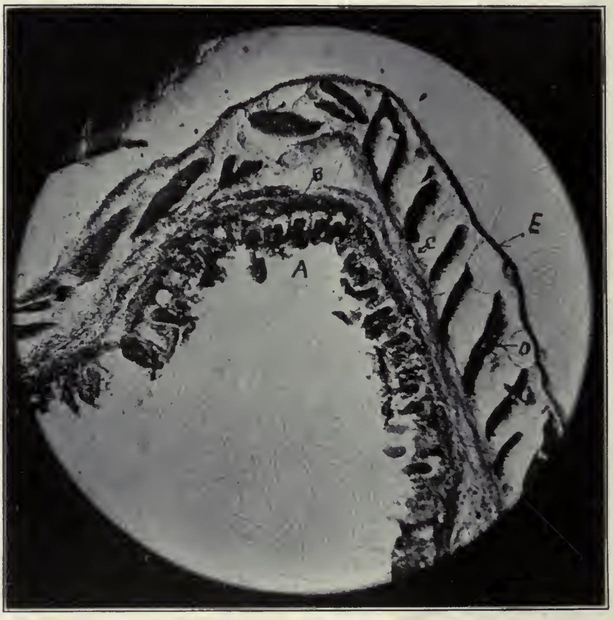

Fig. 3.—Large intestine, low power. Guinea pig, Experiment 5. *A*, mucous coat showing very marked destruction with ulceration and necrosis. *B*, thickening and cellular invasion of submucous coat and very marked edema, *C*, separating the muscle bundles, *D. E.*, serous coat, quite intact.

All animals used for experimentation were carefully selected and of healthy stock; none weighed less than 250 gms. All were given the necessary care to avoid any factors which might disturb or influence the experimental results. All experiments—feeding and inhalation—were conducted simultaneously on two animals of about equal weight; each pair was kept in a separate cage specially designed to permit the collecting of all excreta free from contamination; attention was also paid to the proper temperature, avoidance of draughts, time of feeding, etc.

METHODS OF ANALYSIS

The analytical methods employed to determine the presence or quantity of mercury in organs or excretions were as follows: After a general postmortem examination the organs selected for further study were removed, washed and weighed. A small portion of each was then reserved for imbedding and histologic examination, the remainder was weighed and cut into small pieces for chemical analysis. These pieces were placed in a Kjeldahl flask to which 25 c.c. of concentrated sulphuric acid and about 5 c.c. of concentrated nitric acid were added. This was then heated until

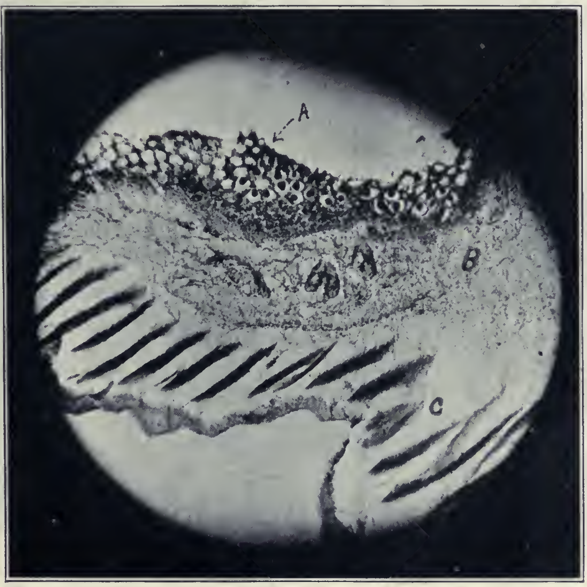

Fig. 4.—Large intestine, low power. Experiment 6 showing practically the same conditions as in Fig. 3, except that the edema is much more pronounced, causing considerable thickening of the whole intestinal wall.

all organic matter had been completely oxidized and digested. To prevent carbonization, the nitric acid was added from time to time. After complete oxidation the contents were allowed to remain standing overnight in the flask; this permitted the precipitation of any remaining insoluble substance. On the next day the fluid substance was diluted and its acidity reduced with ammonia until it was only slightly acid in reaction. Hydrogen sulphid gas was then passed through it until there was complete saturation. A precipitate was thus formed which was filtered out, washed first with hydrogen sulphid and then with alcohol. This was identified as mercury sulphid, dried, weighed and its mercury computed.

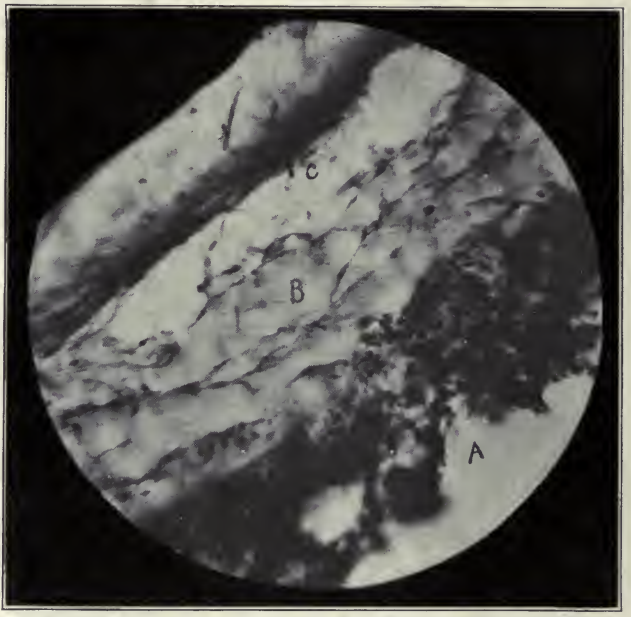

Fig. 5.—Large intestine, high magnification. Experiment 6. Specimen shows the extraordinary edematous state of the submucous layer, *B*, causing a thinning of the fibers and compression of nuclei. *A*, destruction of the mucous layer.

In some of our experiments another somewhat less sensitive analytical method was employed. The first method showed as little as 0.002 gms. of mercury in an organ, while with the second only 0.005 gms. could be detected. In the second method, instead of passing hydrogen sulphid gas through the Kjeldahlized solution, this was first made slightly alkaline with ammonia and later acidified with hydrochloric acid. A few strips of thin copper foil were placed in the fluid, and after warming it, the latter was permitted to stand for about twelve hours. The copper strips were then removed, washed, first with a little water, then with alcohol, and dried in the air. The copper strips were then placed in the bottom of a test tube into which another and smaller tube containing cold water was inserted. The larger test tube with its contained copper foils was then slightly heated. This caused the mercury deposited on the copper strips to become vaporized and to be redeposited in the form of a fine, dusty substance on the outer surface of the inner cold-water-containing test tube. The foil was then removed from the larger outer tube and replaced with a few crystals of iodine. The process was repeated, the smaller test tube being reinserted into the larger, and the latter heated. The heating vaporized the iodine

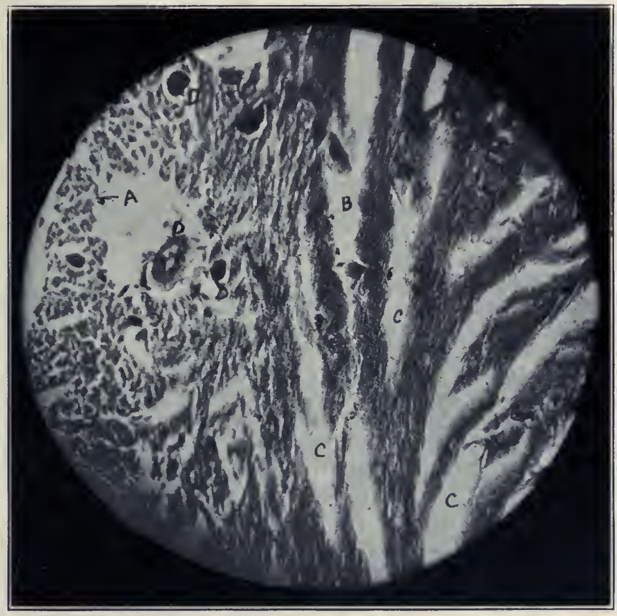

Fig. 6.—Heart, low power. Experiment 8. Section of heart with the muscles cut transversely at *A*, and obliquely at *B*. *C*, separation of muscle bundles and of individual fibers. *D*, blood vessels filled with conglutinated red cells.

which, upon combination with the mercury deposited upon the outer surface of the inner cold tube, caused another deposit to be formed. This new deposit was identified as mercury iodide.

FEEDING EXPERIMENTS

In order to obtain personal acquaintance with the symptomatology due to the effects of mercury upon animals, we began our experiments with *feeding* the drug to them. This enabled us later to judge of and compare these findings with those found in animals subjected to the inhalation of mercurial vapors.

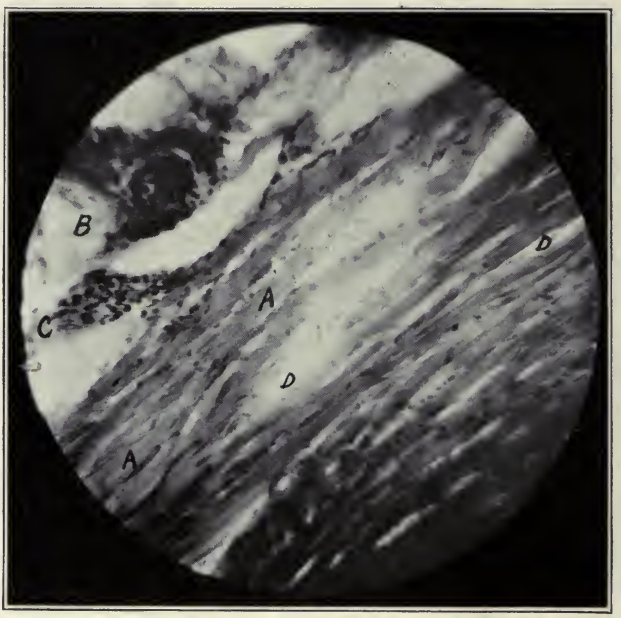

Fig. 7.—Heart, high magnification. Experiment 8. *A*, longitudinal muscle fibers with loss of transverse striations and cloudy swelling. Nuclei, small and compressed by edema, *D*, in the intervening spaces between muscle fibers and bundles. *B* and *C*, small round cell infiltration in the perivascular connective tissue.

Experiment 1.—Two guinea pigs were fed daily with one gm. of metallic mercury finely mixed and ground with zwieback in the proportion of 40 to 60. Both animals succumbed in about four days; the two controls kept under the same conditions and given the same feedings except mercury remained normal.

Experiment 2.—Two guinea pigs were fed daily one-half gm. of metallic mercury triturated with zwieback. Carrots, oats and turnips also made part of their diet. Both animals died in three days. Controls normal.

Experiment 3.—The same feeding was repeated with two other pigs, but with only a quarter instead of a half gm. of metallic mercury. Pig A, of the Angora type, died within three days; Pig B, an animal of the ordinary type, died in seven days. Pig A weighed 555 gm., and after death only 395 gm.; Pig B weighed at the beginning 495 gm., and at death 445 gm.

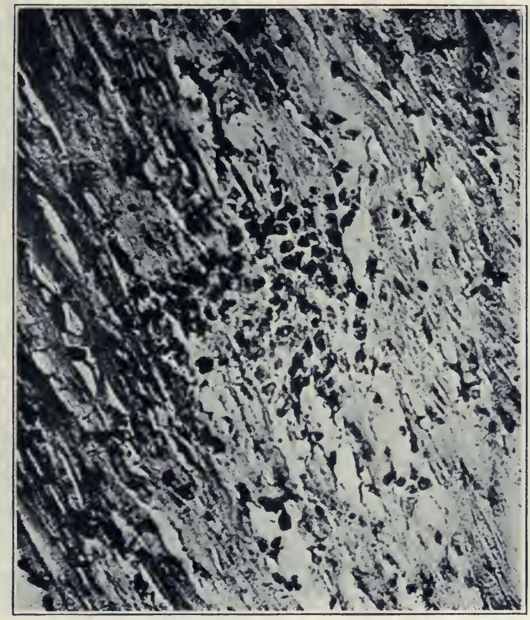

Fig. 7*a*.—Rabbit; eight intramuscular injections with mercurial oil (gray oil). An area of round cell infiltration between the heart muscle fibers. (Kolmer and Lucke.)

Experiment 4.—Experiment 2 was repeated on two other pigs with only one-tenth of a gm. of mercury per day. Death occurred in one animal after six days, in the other after eleven days.

The foregoing experiments served to demonstrate that metallic mercury, if finely triturated in a mortar until its globules are practically invisible, and administered to guinea pigs, causes death. These findings are emphasized because there are on record statements that metallic mercury in its pure form is nonpoisonous, and that even large amounts have been ingested for suicidal purposes, for intestinal obstruction, etc., without any effect upon the organism. This may be true of mercury administered in bulk, but not if it is triturated to very fine globules, as our experiments show.

INHALATION EXPERIMENTS

In the inhalation experiments a cardboard chamber, about 14x14x10″ was used. At the bottom of this was an opening through which a glass chimney of about two inches in diameter projected. The mercury was vaporized at the bottom of the chimney, all vapors entering the chamber through it. Each pair of animals was placed in the chamber for simultaneous treatment and was kept there until no visible mercury vapor remained, which occurred usually in about twenty minutes. For vaporization only pure metallic mercury was

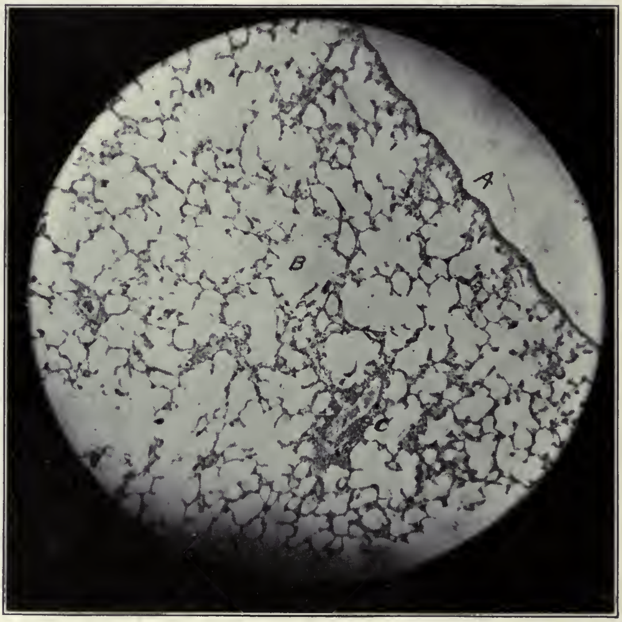

Fig. 8.—Lung, low power. Experiment 14. Mercury inhalations with a fair supply of fresh air administered to guinea pig every third day. *A,* pleura slightly thickened. *B,* lung parenchyma with fairly normal alveolar spaces and walls. In some places evidences of slight thickening and cellular invasion of alveolar walls. Blood vessels congested, some with a moderate tendency toward perivascular small cell infiltration, *C.*

used because vaporization of its compounds, as was long ago proved, results in the formation of other substances most of which are deleterious to the organism. The sulphides, chlorides, oxides and other mercury compounds are very injurious, as they produce noxious gases (SO_2, Cl, etc.) which, when inhaled, are very irritating and destructive to the tissues; they are productive of by-effects which interfere with the action of mercury. As the purpose of these experiments was to determine the effects of mercury inhalations, pure and simple, it was deemed best to limit ourselves to the vaporization of pure metallic mercury excluding all of its combinations. To assure the complete oxidation and vaporization of the metallic mercury, this was mixed with an oxidizing agent and other inert material, both, however, of a completely innocuous character. This mixture was utilized for the generation of mercury vapors; it was placed in the chimney, ignited, and the vapor directed into the inhalation chamber.

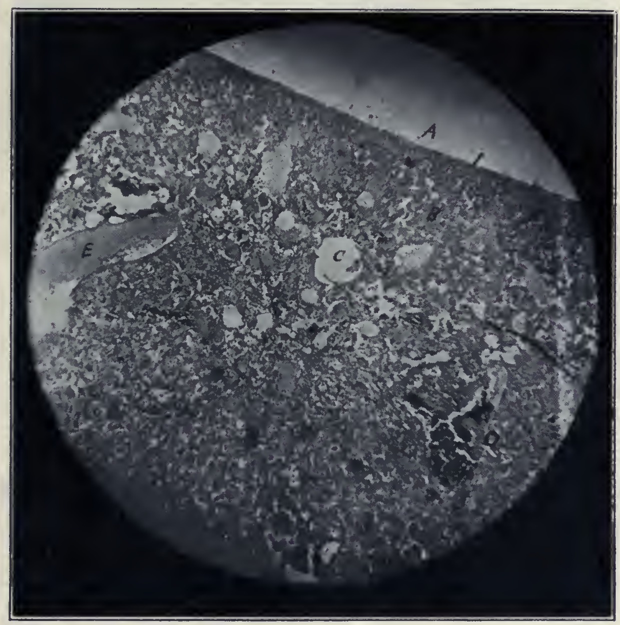

Fig. 9.—Lung, lower power. Experiment 18. Inhalations of mercury without free supply of fresh air. *A*, pleura intact but somewhat thickened. *B*, lung parenchyma very markedly changed; most of the alveolar spaces are airless and filled with hyaline substance, desquamated epithelia and other substances of hepatization. Numerous hemorrhagic areas here and there. Very few clear alveolar air spaces, *C*. *D*, blood vessels very much congested with destroyed red blood cells.

Some of the animals were given fumigations daily; others got the vapor twice a day or on alternate days. The dosage was varied; the dilution of the vapors with air was also modified with the object of varying its concentration.

Experiment 5.—Two guinea pigs were given by inhalation, once daily, two gm. of metallic mercury. Death occurred in four days. Combined weight at the beginning 660 gm., at the end 510 gm. Mercury discovered in the excretions only on the fourth day.

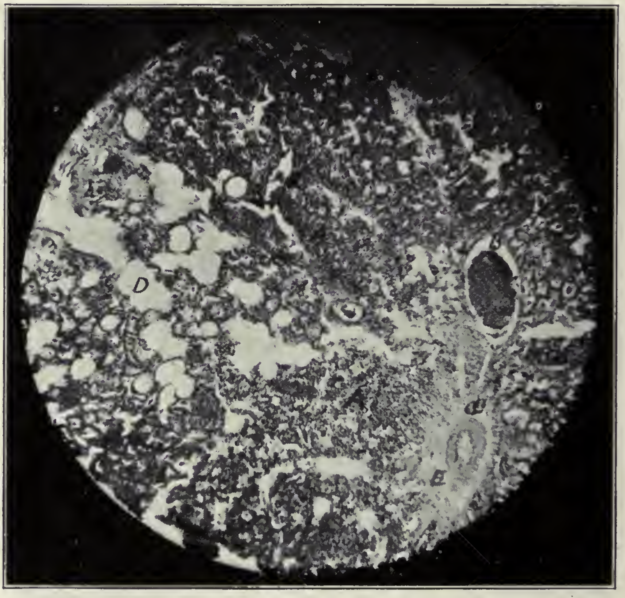

Fig. 10.—Lung, low power. Experiment 15. Mercury inhalations with moderate fresh air supply, showing very intense affection, most of alveolar air spaces being obliterated, but not to an extent observed in the previous specimen (Fig. 9). Many of the air spaces show a compensatory emphysema, others are only partially filled. Blood vessels, *B*, filled with conglutinated red cells.

Experiment 6.—Two guinea pigs were given inhalations twice daily, two gm. at each treatment. Death occurred in three days. Mercury found in excretions only on the last day. Combined weight at start 630 gm., at the end 575 gm.

Experiment 7.—Two pigs were administered half gram doses daily. Death occurred in seven days. Combined weight 605 gm., at end 470 gm. Mercury in the excretions on the second day, also on the fourth and seventh days.

Experiment 8.—Two pigs were treated in the foregoing manner with half a gm. of metallic mercury daily, but administered in two inhalations. Death occurred on the sixth day. Combined weight at first 715 gm., at the end 645 gm.

Experiment 9.—Two animals were treated with the same quantity of mercury administered in three inhalations. Combined weight 540 gm., at the end 476 gm. The death of one occurred in five, of the other in six days.

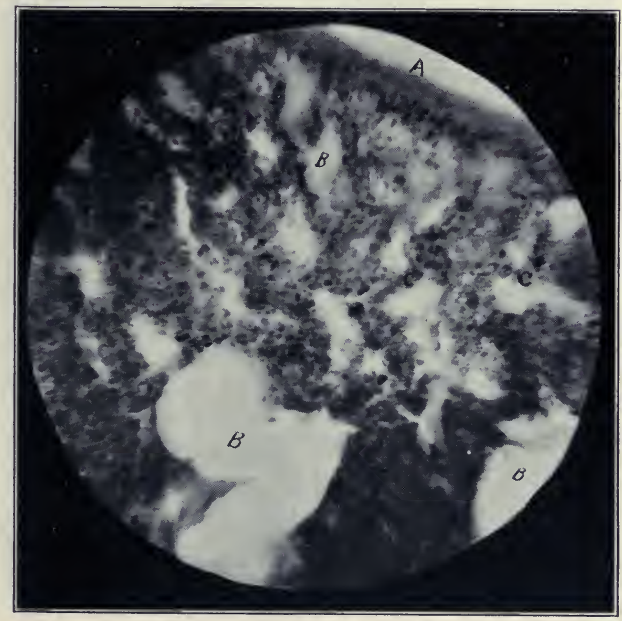

Fig. 11.—Lung, high power of specimen, Fig. 10. *A*, thickened pleural coat. *B*, air spaces, most of them of diminished air volume and compressed by the strongly congested alveolar capillary vessels; others showing compensatory dilatation, while others again are filled with hyaline substance, and desquamated epithelia.

Experiment 10.—Two animals were treated with one gm. of mercury evaporated in the manner used in the preceding experiments, but the fumigation chamber was a metal one. The animals died on the eighth day. The excreta failed to reveal mercury. The walls of the chamber were covered with a mercury amalgam.

Experiment 11.—A rabbit weighing 1550 gm. was given eleven inhalations; for the first three days twice daily, and once for the subsequent five days. It succumbed on the seventh day weighing 1420 gms.

Experiments 12-20.—These experiments were similar to those already described, except that the amount of air admitted into the inhalation chamber was regulated, so as to dilute or concentrate the mercury vapor to be inhaled.

In all over fifty animals were used, in the feeding and inhalation experiments. Those succumbing to extraneous causes not connected with our studies were not included. For verification many experiments were frequently repeated.

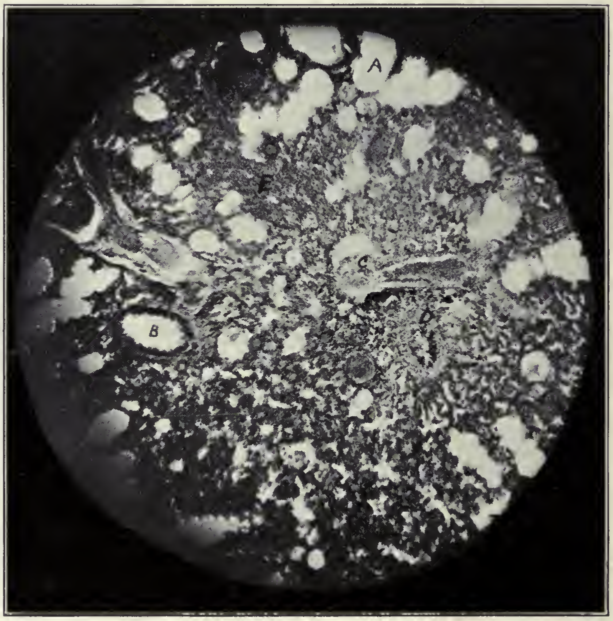

Fig. 12.—Lung, low power. Another view of previous specimen, showing also a thickening of the walls and irregularity of bronchus, *B*. *C* and *D*, engorged blood vessels with altered blood corpuscles.

SYMPTOMATOLOGY

While in the inhalation chamber the animals endeavored to keep away from the entering fumes. Sniffing, sneezing and restlessness were at times observed. Beginning with the second day they appeared to lose their appetite, first neglecting and later refusing food altogether. They soon showed lack of activity, became apathetic and depressed and permitted themselves to be handled without resistance. Their faces showed fullness in the parotid region and later distinct puffiness and swelling; the eyes became dull and lustreless, and sank deeper and deeper as the end approached. Dropping of saliva from the mouth was more common in the animals fed on mercury than in those inhaling the drug. There was considerable loss of weight in all; indeed, marked emaciation and loss of muscular tone were distinct features. The fur lost its richness, and shedding of hair became conspicuous. In some instances the volume of urine was increased, but in the greater number of cases it was diminished. The feces of all animals given mercury by feeding and inhalation were semisolid and bloody. Urine and feces contained mercury in nearly all instances except in those where death occurred very early in the process of experimentation. Mercury was not necessarily present in the excretions every day; in some instances it was found in the excreta early, in others late, perhaps

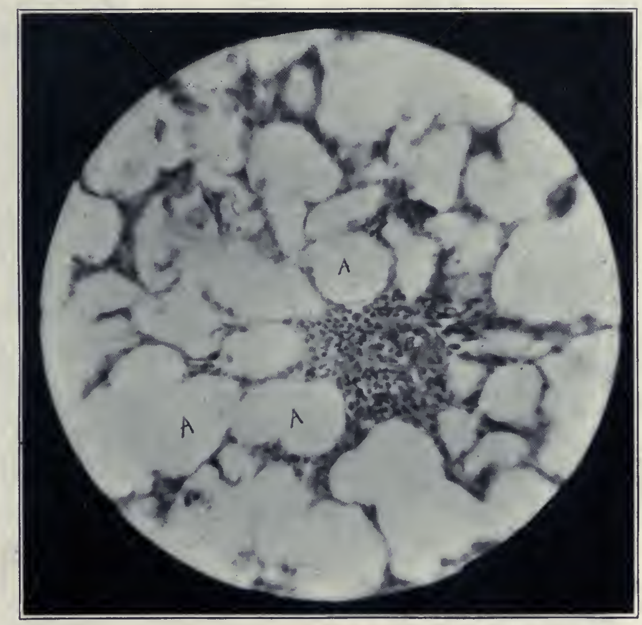

Fig. 13.—Lung, high magnification. Experiment 14, showing blood vessel, *B*, with considerable perivascular cellular infiltration.

on the last day; in others it varied from day to day. Twitching of the muscles, weakness of extremities, and a state of pseudoparalysis and convulsions sometimes preceded death. The duration of life did not seem to be dependent upon the total quantity of mercury inhaled, but rather upon the frequency of administration and the concentration of vapor. The severity of symptoms was also independent of the absolute quantity.

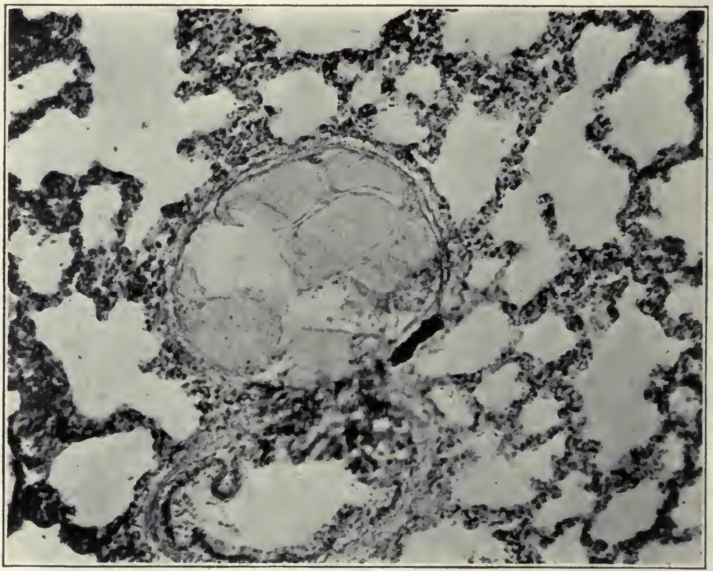

Fig. 13*a*.—Rabbit; twelve intramuscular injections with mercuric chloride. Lung: A medium-sized vein contains a canalized thrombus, the new canal being lined by endothelium; a few newly formed capillaries are present within the mass of blood. (Kolmer and Lucke.)

GROSS POSTMORTEM FINDINGS

Since no striking differences were observed in the gross appearances of organs in the two classes of experiments, the gross pathologic description refers to the organs of all animals—those fed with mercury or subjected to its inhalation. The most striking changes were observed in the gastrointestinal tract. Here the mucous membrane was found to be very markedly congested and in places very much inflamed. The intestinal wall was in some instances so atrophied and destroyed that it appeared as thin as tissue paper. There, also, single and multiple deep, yellowish gray ulcers were encountered, some pin point, others more extensive; some very deep and large, others more superficial. These were found principally in the cecum and sigmoid but not infrequently also in the descending colon. In one case a large ulcer was discovered in the stomach. The small intestines seemed to be free from deep ulcerations, but marked discoloration and erosions of its mucosa were present. Intestinal contents in almost all cases were bloody, mucoid and in general resembled the feces in severe dysentery.

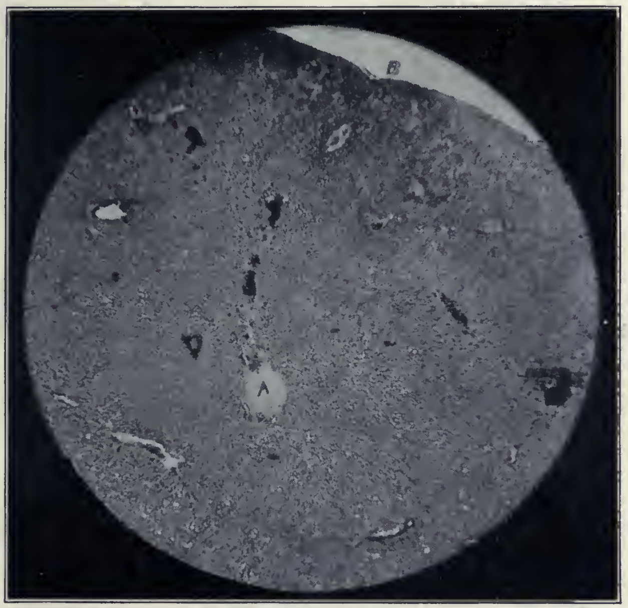

Fig. 14.—Lung, low power. *A*, interlobular vessels distended with agglutinated blood or clear albuminous hyaline substance. *B*, normal capsule. *C*, liver parenchyma, studded throughout with small congested intralobular vessels and fatty degenerated cells.

The kidneys were soft and large, with markings blurred and otherwise showed evidences of parenchymatous changes. The heart muscle showed some degeneration, and in one of the worst cases there were marked pericardial adhesions; in this case very extensive pleuritic adhesions, involving especially the left lung, were also present.

The pulmonary tissues shared in the general congestion of all organs, but in those cases where inhalations were forced and given very frequently, the lungs contained in addition hemorrhagic infarctions, areas of consolidation and similar evidences of severe affection. The bronchial and tracheal mucosa showed similar signs of congestion, thickening and catarrhal inflammation. The spleen was found to be congested, the liver soft and friable, the ribs thin and showing medullary degeneration. The adrenals were much congested. The brain and spinal cord showed moderate congestion but appeared to be free from any marked macroscopic pathologic changes.

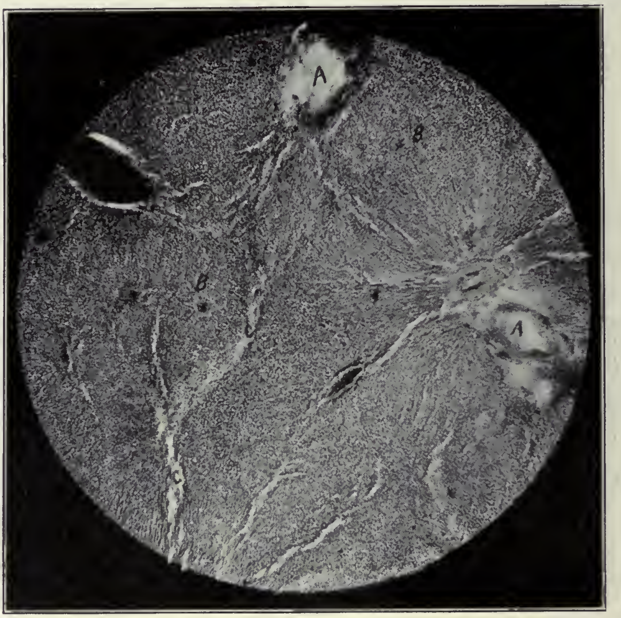

Fig. 15.—Liver, low power. Experiment 6, showing very extreme distention of all blood vessels intralobular, capillaries, etc.

MICROSCOPIC OBSERVATIONS

The microscopic descriptions refer only to organs obtained from animals subjected to inhalations and not to organs examined after feeding mercury. It seemed unnecessary to describe the histologic changes resulting from our feeding experiments as adequate data recording the pathology of such organs are in existence. Soon after the death of the animal the organs to be studied were placed in a solution consisting of equal parts of Mueller's fluid and 10 per cent formalin solution, where they remained for several days, after which they were imbedded in paraffin, sectioned and stained with hemotoxylin and eosin for microscopic study.

The following organs were investigated: Esophagus, small intestines, large intestines, liver, spleen, kidney, adrenal glands, cerebrum, cerebellum, spinal cord, heart and lungs. The stomach, except in one case, presented so few macroscopic changes that histologic studies seemed uncalled for. A number of sections were made from each organ of every animal dissected.

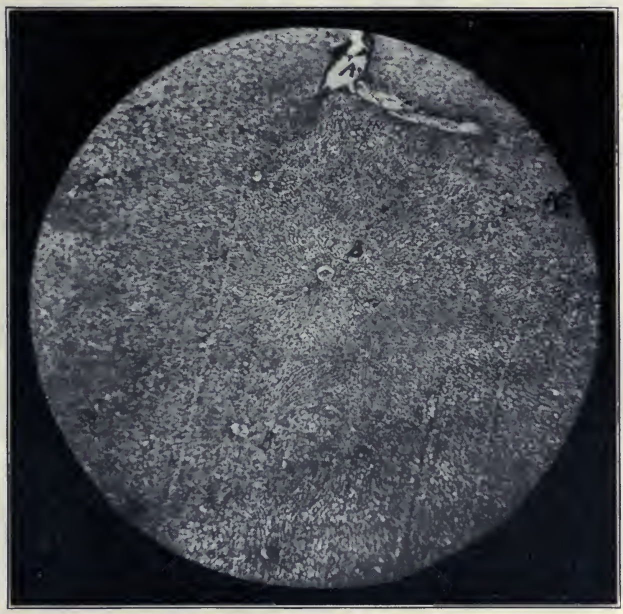

Fig. 16.—Liver, low power. Experiment 15. *A*, parenchyma permeated throughout by extremely distended capillaries of lobules; liver cells show fatty degeneration and cloudy swelling. Hemosiderine pigment also quite extensive.

The histologic description which follows is based upon the combined study of all similar organs, the object being to avoid the repetition that a description of the results of every experiment would entail. The organs of animals subjected to various mercurial manipulations differed so slightly in their final gross and microscopic appearances that a separate description of each seems unnecessary. Whether the animals succumbed slowly or more rapidly depended on the method of mercury administration; the character of the final pathologic changes, however, was identical, the destructive effects differed only in degree.

The following histologic changes were observed in the organs studied:

Esophagus.—The stratified epithelial layer of the mucosa presented a moderate degree of cellular cloudy swelling; covering the epithelium was a layer of hyaline structureless eosin-staining material. The tunica propria appeared to be somewhat edematous, its blood vessels congested. There were no apparent changes in the muscularis mucosa, the external and internal muscular layers. The submucous coat appeared markedly edematous and in some places showed a moderate degree of cellular infiltration. The lymph nodules appeared normal. The blood vessels of the adventitious coat were distended.

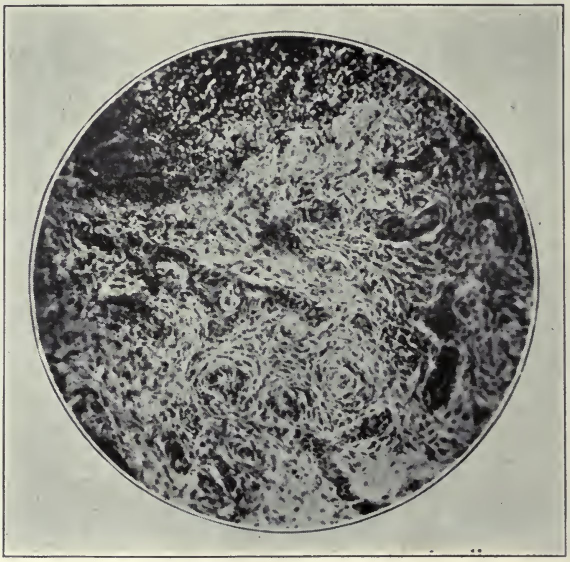

Fig. 16*a*.—Rabbit; thirty-five doses by mouth of yellow mercurous iodide. Liver: An area of periportal connective tissue proliferation, small round cell infiltration. The biliary ducts are considerably increased in numbers. (Kolmer and Lucke.)

Small Intestines.—The epithelial layer of the villi and other parts of the intestinal mucosa were in some places intact, in others partially ulcerated and even entirely destroyed; in some places it was found loosened from its underlying connective tissue, having hyaline substance or loose blood cells in the spaces. There was in places marked cellular infiltration of the tunica propria. The blood vessels here were very much congested; lymph spaces were widened. The connective tissue in some parts showed a tendency toward cell-proliferation. The smooth muscle fibers of the submuscularis appeared compressed, their nuclei stained less intensely than normal. The longitudinal and transverse muscular layers presented very little change. All blood vessels were distended with agglutinated red blood corpuscles. The subserous coat also showed some thickening and cellular infiltration, the serous was in places interrupted.

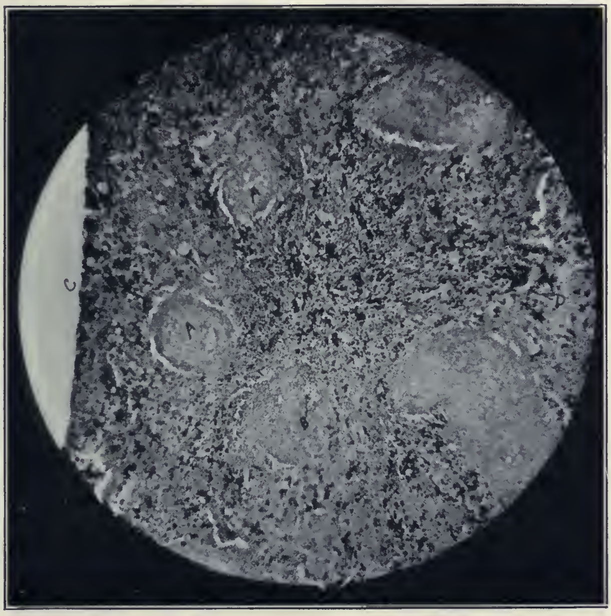

Fig. 17.—Spleen, low power. Experiment 6. Very marked hemosiderosis throughout parenchyma except follicles, *A*, which appear to be perfectly normal with arterial walls, *B*, not infiltrated. *C*, capsule very thin. Trabeculae well defined, occasionally small thrombotic areas.

Large Intestines.—The microscopic appearance of the large intestines differed on the whole but little from that of the small, with the exception that in some places the ulcerative processes were much more accentuated. Marked ulceration of the epithelial layer was quite evident; partial destruction and shedding of epithelium was a common feature. The glandular cells were shrunken, with loss of outlines and nuclei indistinct. Blood extravasations were frequently found in the tunica propria and elsewhere; the blood vessels showed marked congestion. The submucous layer was very edematous, the edema also invading the muscularis and separating the individual fibers very appreciably. The outer muscle coats showed no special changes; the subperitoneal layer appeared to be thickened, the connective tissue fibers edematous.

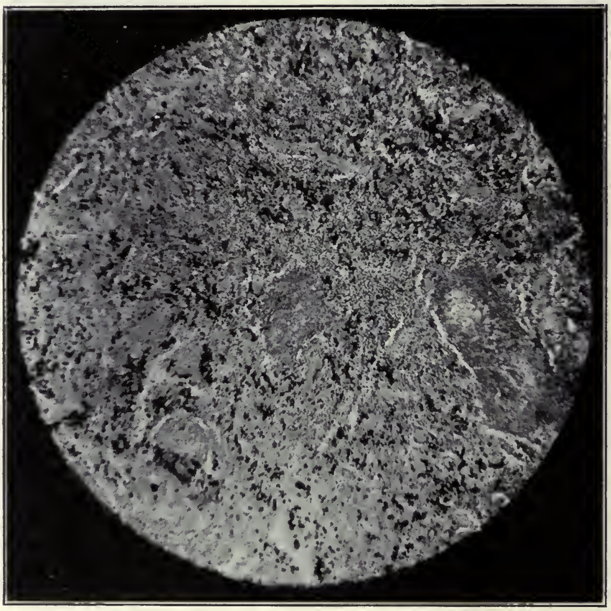

Fig. 18.—Spleen, low power. Experiment 18, showing the same changes as in Fig. 17. Hemosiderosis is more marked. Vascular engorgement also prominent.

Heart.—The pericardium and endocardium appeared mostly normal. The myocardium presented general cloudy swelling of the cell sarcoplasm with partial loss of striations, mostly of the transverse markings. The muscle fibers appeared to be compressed in some places, with their nuclei thinned and staining rather faintly; but in general the staining of muscle fibers and nuclei was normal. The muscle bundles were separated by edema and in a few instances rupture of capillaries, with resulting small focal hemorrhages between muscle bundles, was observed. All capillaries were intensely congested and filled mostly with agglutinated red cells. The interstitial tissues showed no special increase or cellular infiltration except in two instances. There were no evidences of perivascular infiltration.

Lungs.—The pathology of the lung tissue, because of its direct contact with the mercury vapors, was of especial interest. The changes here differed greatly and were concomitant with the manner in which the mercurial vapors were administered. In the animals treated radically, i.e., where the vapors were administered frequently and in concentrated form, the pathologic changes were extremely marked; while in those to whom the mercury was administered at rare intervals, on alternate days or less frequently, and in less concentrated form with plenty of fresh air accompanying it, the pathologic changes in the respiratory tract were very insignificant. In these only a moderate degree of congestion or capillary engorgement, epithelial desquamation and other minor changes were observed. In the severer cases the effects were pro-

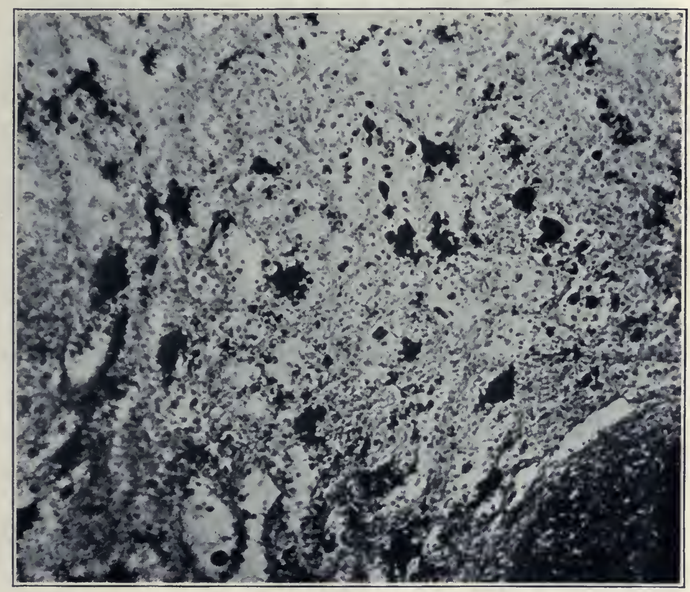

Fig. 18*a*.—Rabbit; four intramuscular injections with calomel. Spleen: Considerable hemosiderosis is present (black in photograph). The hemosiderin granules occur as fine particles within phagocytic cells and as coarser granules free in the tissue. Some animals of other series presented a more marked pigmentation. (Kolmer and Lucke.)

found. Here the alveolar walls were so engorged with blood as to practically obliterate the spaces; these were filled either with desquamated epithelium and blood cells, or with hyaline substance. Most of the blood vessels contained thrombotic masses. Patches of consolidation, infarction, and similar severe processes were common. In some places local collapse was observed; in others small round cell infiltration of a slight degree was evident. The bronchi also were the seat of marked inflammatory changes and of moderate round cell infiltration of their walls. The pleura in most cases appeared to be normal except where the pulmonary pathologic changes were severe. There were nowhere evidences of pulmonary abscesses or of empyema.

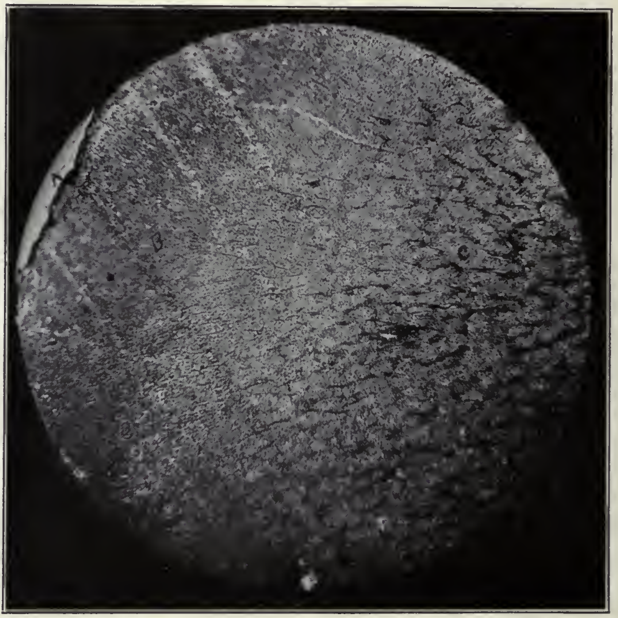

Fig. 19.—Suprarenal gland, low power. Very marked distention of all blood vessels, especially those of the medullary portion, *C.* *B,* cortical portion, showing no pathologic changes of parenchyma. *A,* normal capsule.

Kidneys.—The capsule was generally found to be thinned out, but free from definite vascular or cellular changes. The most extensive injuries of this organ were confined almost exclusively to the cortical layer of the parenchyma; its convoluted tubules appeared to be most affected. These showed all changes of involvement, from mild cloudy swelling to complete necrosis. In some instances the cells presented only slight swelling with moderate granular changes and perhaps here and there an anuclear cell. In others the changes were quite pronounced; here the morphologic integrity of the cells was found to be completely destroyed, with nuclei either absent or staining very poorly. Fatty vacuolation was very common. The lumen of the tubules was most frequently obliterated and filled either with acid-staining material or finely granular albuminous substance. At times desquamated cells or casts were observed in the lumina of the larger tubules.

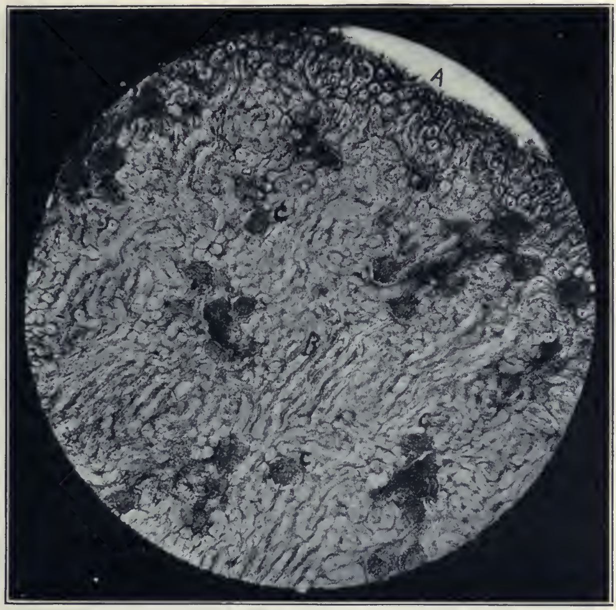

Fig. 20.— Kidney, low power. Experiment 7. Cortex, showing very marked changes in its tubular portion, *B*. Also extreme congestion of glomerular bodies as well as congestion of all other vessels especially subcapsular, *A*.

The glomerular structures were very markedly congested; the capillary tufts distended with agglutinated cells. At times these tufts were separated from the capsule and the spaces filled with some hyaline or granular material. Pericapsular thickening or infiltration was not very much in evidence, Henle's tubules did not seem to be changed to any appreciable extent. In some of the collecting tubules a little desquamation or loose epithelia were here and there observed; otherwise these appeared to be normal. In some of the slides showing extensive kidney affection, infarctions were present, and all blood vessels from the smallest to the largest were very much engorged; some also contained thrombi.

Liver.—The liver capsule presented nothing interesting. The serous layer was smooth and uninterrupted, the subserous neither thickened nor edematous. The interlobular vessels were found to be very much congested and filled sometimes with well-preserved but more commonly with agglutinated red cells. The central lobular vessels and capillaries were prominently distended, some with fairly well preserved red cells, but more frequently with cells more or less fused. Sometimes the peripheral vessels, the branches of the hepatic artery and portal veins and their capillaries were likewise distended, while the central lobular veins and adjacent capillaries seemed almost empty.

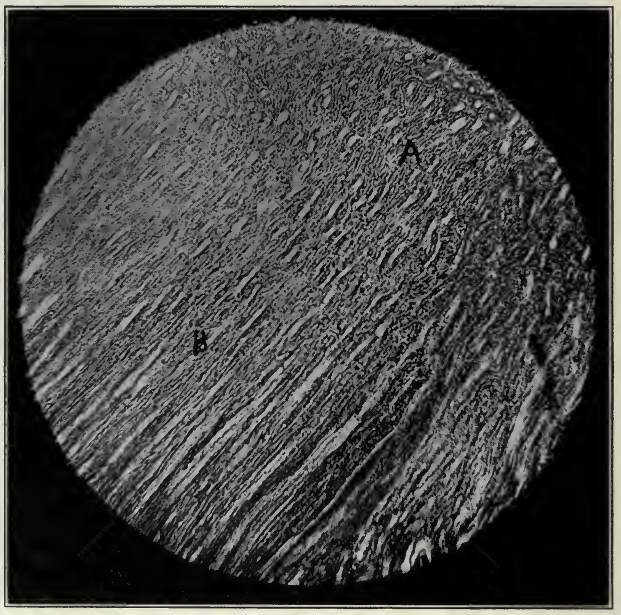

Fig. 21.—Kidney, low power. Experiment 7. Medulla, showing very little change except marked congestion of blood vessels. The collecting tubules and ascending limbs of Henle's tubes show no particular pathologic changes.

The parenchyma cells were mostly in a state of cloudy swelling, but many also showed fatty degeneration; their protoplasm was slightly granular, the nuclei stained poorly; some were pycnotic. The peripheral tissues seemed to be somewhat increased in volume and occasionally infiltrated with small cells. The bile ducts did not seem to show any change. Pigment was present here and there but not to any appreciable excess.

Spleen.—The capsule was rather thin in most places; the follicles were but rarely well defined, so that at times they appeared to coalesce with the pulp proper. There was intense congestion and numerous red cell thrombi in various parts of the organ. The trabeculae were well defined. Considerable pigment was observed throughout the splenic parenchyma.

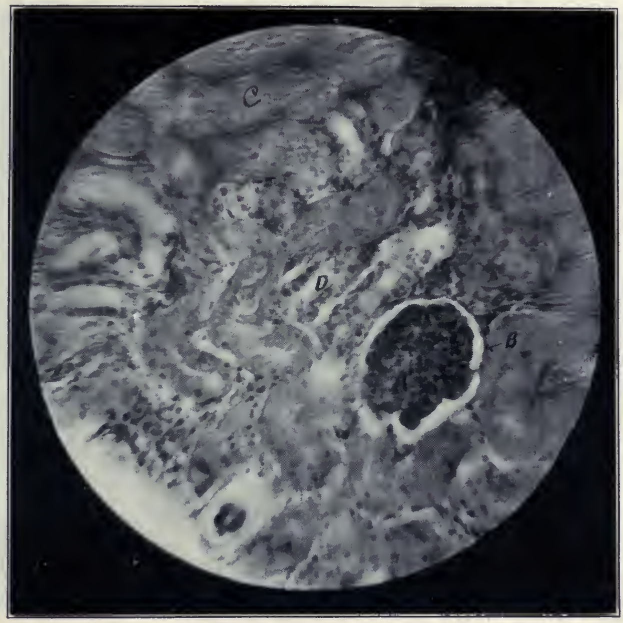

Fig. 22.—Kidney, high power. Experiment 7. *A,* marked distention of glomerular bodies with agglutinated red cells. *B,* Bowman's capsule. *C,* convoluted tubules with complete effacement of cellular outline, with either absence or indistinctness of nuclei and complete obliteration of lumen. *D,* collecting tubules containing debris, desquamated epithelia and at times casts.

Adrenals.—These appeared to be very little changed except that the blood vessels in the medullary portion were very much distended; some also contained thrombi or agglutinated red cells. The capsule was of normal thickness; the cortical cells mildly swollen.

Brain and Spinal Cord.—In no section of the cerebrum, cerebellum and spinal cord were striking pathologic changes to be observed. There was a general vascular engorgement noticeable in many of the slides, and thrombi of conglutinated erythrocytes or of hyaline masses were occasionally seen. No gangrenous or markedly infiltrated areas were observed.

Summary.—A summary of the microscopic study of the individual organs may be stated briefly in the following conclusions: All organs showed very marked congestion and distention of blood vessels with either thrombi, granular substance or agglutinated red cells. There was cloudy swelling of the cellular tissues of almost all the parenchymatous organs (liver, spleen, adrenals, etc.). There was ulceration and severe destruction of the intestinal mucosa. There was cloudy swelling, fatty degeneration and even necrosis of the kidneys. All organs showed signs corresponding to the symptoms of a general toxemia.

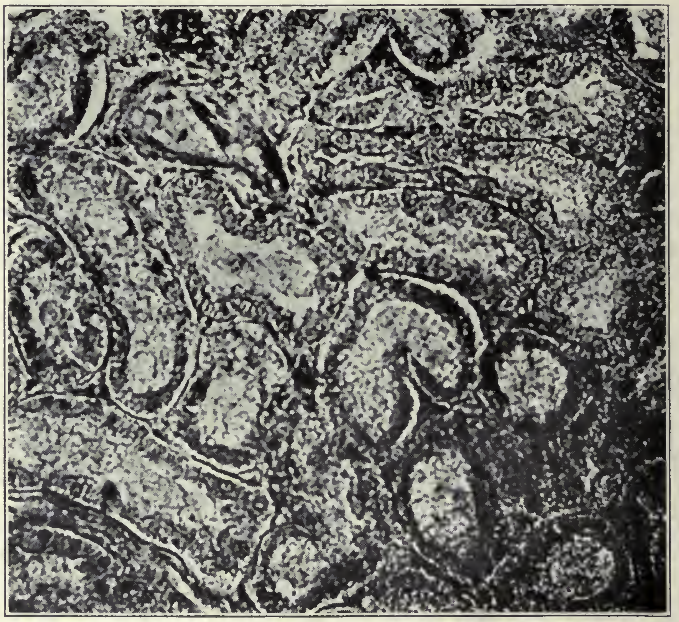

Fig. 22*a*.—Rabbit; eighteen inunctions with mercurial ointment (gray ointment). Kidney: Shrinkage of the epithelium of the convoluted tubules because of fatty "degeneration." The lumina are filled with granular, eosin-staining debris. (Kolmer and Lucke.)

OBSERVATIONS OF OTHER INVESTIGATORS

A careful review of the literature offers but little information concerning the pathology of mercurial inhalations. Merget[1] found that in some of his experiments with rabbits and pigeons no visible alterations could be detected in any of the animal organs, but their chemical analysis disclosed mercury. This he found to be distributed as follows: kidneys, liver, lungs, brain and cord, heart, muscle and bones; the latter organs contained only traces, too small to be determined. He also found mercury in the excreta of all animals treated, after the second day. The apparent integrity of the tissues in which he found no visible alterations made the cause of death seem problematic. Without being able to explain the toxicity he believed that the mercury vapors were lethal through their influence upon the nervous system.

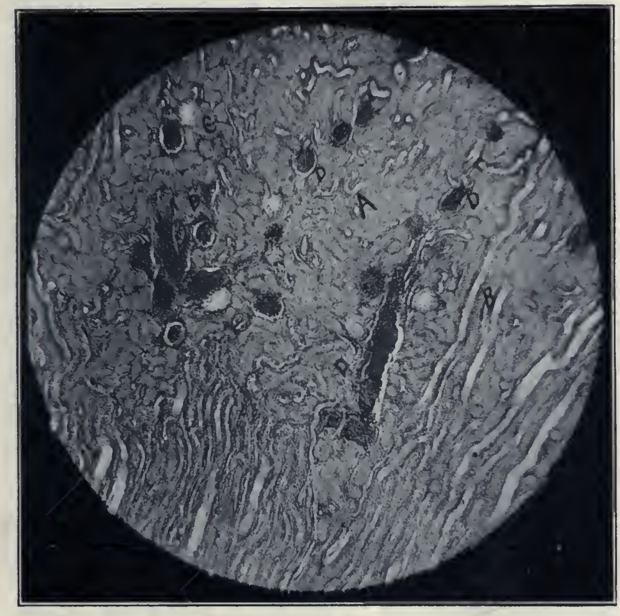

Fig. 23.—Kidney, low power. Medullary portion. Experiment 8, exhibiting the same pathologic changes as Fig. 20, Experiment 7. Archiform veins greatly distended.

As to the symptoms, Merget observed that respiration was slowed, the urine increased in density and amount; there was slight tachycardia, low fever, leucocytosis and marked emaciation. He also states that when toxic effects arise from continuous respiration of air saturated with mercury vapor, these always kill the animal exposed to it, the more rapidly the smaller the mass of the animal, and that death is preceded by a series of nervous troubles, the only ones which appear; in the higher animals these appear later, develop more slowly and are less dangerous than in fishes and amphibia. He also records that when the degree of saturation is sufficiently low, mercurial vapors cease to be toxic, even though they be breathed continuously, or, though saturated, the vapors are nontoxic if absorbed intermittently by respiration.

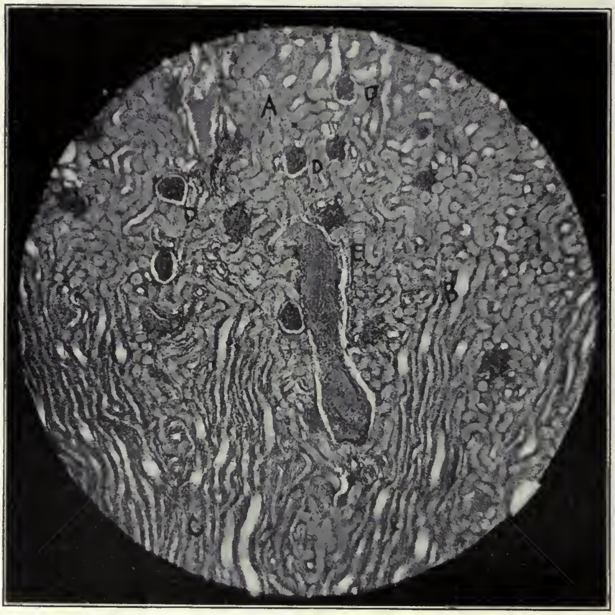

Fig. 24.—Kidney, low power. Same experiment showing some of the cortical ray tubules affected in a similar manner as the convoluted.

Our experiments seem to bear out the observations of Merget. Mercury was found in almost every organ analyzed for its presence. Even in the cerebrospinal system which microscopically did not appear to show any particular structural changes mercury was present. Whether the mercury found there by chemical analysis was derived from the nerve tissue proper or the blood of its congested vessels, cannot be here stated, but inasmuch as the nerve tissues presented so little pathologic change, it seems plausible that the mercury found was derived from their blood supply. Our observations also verify Merget's experience that the toxicity of mercury vapor depends upon the concentration, the method of administration, the extent and frequency of exposure, the size, age, and nature of the animal.

Von Baerensprung[2] found droplets of mercury in consolidated areas of the lungs of rabbits exposed to boiling mercury or to the vapors arising from open dishes containing this element. He also found in these animals irritation, congestion and even consolidation of the air passages and lungs.

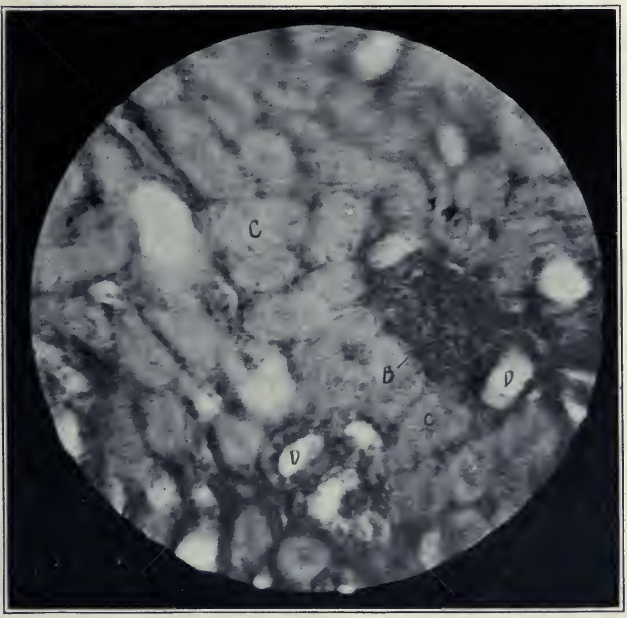

Fig. 25.—Kidney, high power. Experiment 18, showing the very intense degenerative changes affecting the cells of convoluted tubules, *C*. Lumina completely occluded, with cell outlines and nuclei absent. Glomerulus, *A*, extremely congested and filled with degenerated red cells. *D*, collecting tubules and parts of ascending limbs of Henle show little change.

D'Eulenberg[3] experimented with boiling mercury and showed that mercury could be found in the air passages and gastrointestinal tract, in the latter only in quantities which were negligible in proportion to those found in the lungs. The pathologic changes observed in the respiratory tract were mostly those of congestion.

Darrien[4] states that in all mercury intoxications by means of mercury salts there are nerve cell lesions, particularly in the cells of the anterior horn of the cord. In the cells, the chromatophil substance becomes finely granular and may even disappear completely.

Skudro[5] found acute hemorrhagic inflammation in the lungs and degeneration of kidneys in mice exposed to the vapors from gray ointment.

Ricker and Hesse[6] found the principal lesions in animals inhaling vapors from gray ointment to be in the lungs, and to consist of hyperemia with or without hemorrhages and inflammation. Inflammation was also observed by them in the kidneys and colon.

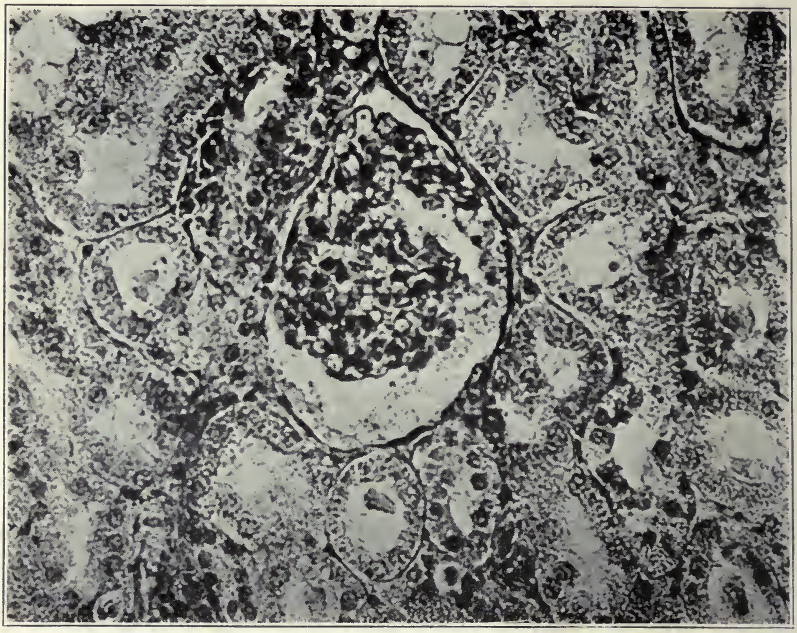

Fig. 25*a*.—Rabbit; eight intramuscular injections with mercuric chloride. Kidney: The capsular space and the lumina of several of the collecting tubules contain granular, eosin-staining material. The lining cells of the capsule are slightly swollen; the epithelium of the convoluted tubules is cloudy, swollen, often vacuolated and frequently anuclear. (Kolmer and Lucke.)

INVESTIGATIONS OF KOLMER AND LUCKE

The best and most extensive study of the effects of mercury upon the animal organism has been made by Kolmer and Lucke.[7] These investigators have recently published a very comprehensive analysis of the end-results of the two common drugs used in the treatment of syphilis—arsenic and mercury. Their investigations were conducted especially to determine the pathologic effects produced upon all the vital organs by these two drugs administered in their various forms and by all the common routes. Their mercury experiments comprise a careful histologic study of organs of rabbits subjected to different forms of this drug, administered in every way but by inhalation. One series of animals they injected with *insoluble* mercurials. They injected, intramuscularly, salicylate of mercury and olive oil in doses of 0.002 gm. per kilo. of weight, which is equivalent to 0.0201 gm. or about two grains per 60 kilos. or 130 lbs. The injections were made at intervals of one week into the muscles of the thighs. To another set of animals they gave calomel in sterile oil, in the same amount, as the mercury salicylate; to a third set mercurial oil was given, also in the same amount and manner.

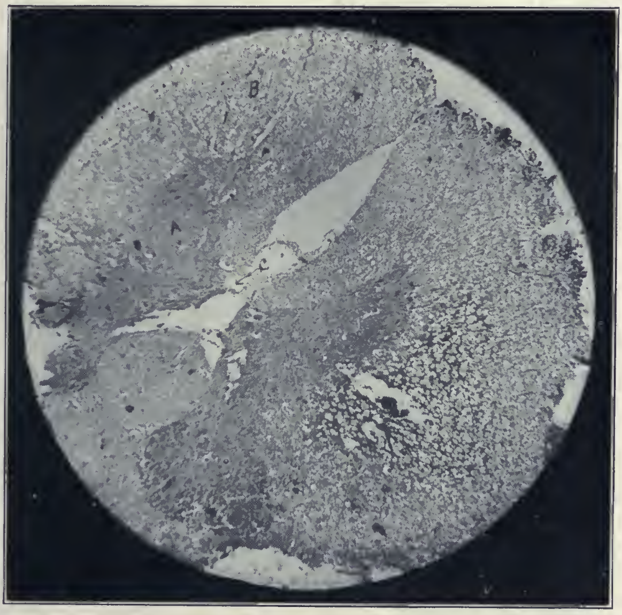

Fig. 26.—Spinal cord, low power. *A*, Medullary portion. *B*, cortical portion, both free from serious pathologic changes except vascular congestion. *C*, central canal.

Other experiments they conducted with *soluble* preparations of mercury injected intramuscularly. Three rabbits were given, three times a week, 0.0004 gm. of mercury chloride per kilo. of weight, an amount equivalent to 0.024 gm., or about one-third of a grain per 60 kilos. or 130 pounds. Three other rabbits received 0.0005 gm. of benzoate of mercury, equivalent to 0.03 gm. or about one-half of a grain per 60 kilos., or 130 pounds.

They also gave to three rabbits *intravenous* injections of mercuric chloride every five days, in doses of 0.0002 gm. per kilo of weight, equivalent to 0.012 gm. or one-fifth of a grain per 60 kilos., or 130 pounds. In three rabbits mercury cyanide and in three others mercurophen was injected in the same doses.

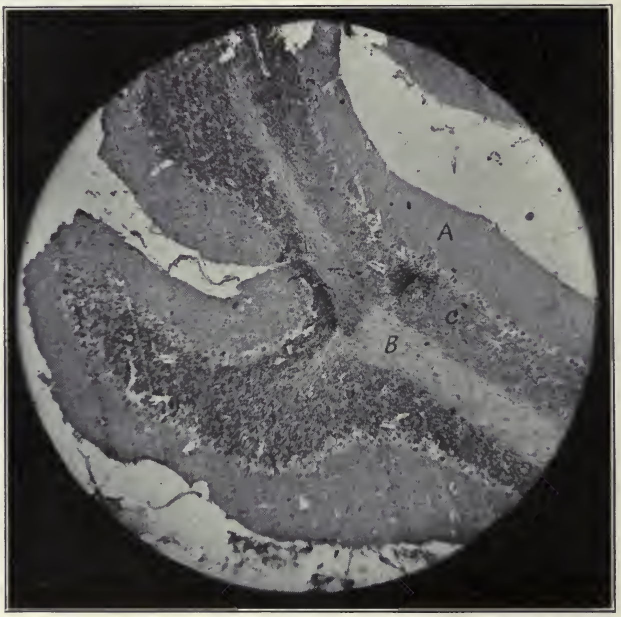

Fig. 27.—Cerebellum, low power. Practically normal cortex, *A*, and medulla, *B*. The ganglionic and granular strata negative.

The effects of yellow mercurous iodide given in *pill form* daily in doses of 0.002 gm. per kilo. of weight, corresponding to 0.120 gm. or two grains per 60 kilos. or about 130 pounds, were also studied by these authors.

Finally they studied the effects of *inunctions*. They employed upon one set of rabbits a 50 per cent gray ointment, using 0.09

grams per kilo. of body weight, corresponding to 5.4 gm. or about 1½ drams per 60 kilos., or 130 pounds. This was rubbed in daily for ten minutes; to another set of rabbits similar inunctions were given with a 50 per cent calomel ointment.

Much credit and appreciation is due to Kolmer and Lucke for the very accurate, exhaustive and excellently presented study of a subject which is a very timely one. Very little was known of the morphological effects of the arsenicals and mercurials upon the animal organism until their work appeared. Until then the structural consequences of many mercurials given singly or in multiple combinations were unknown. From work so conclusive it is very interesting to learn that in all their experiments, although the mercury was administered in every commonly employed form and by all ordinary routes, the effects of the drug upon the tissues were similar and varied only in minor details, in extent and degree. The pathologic changes were in all cases identical and characteristic for each organ.

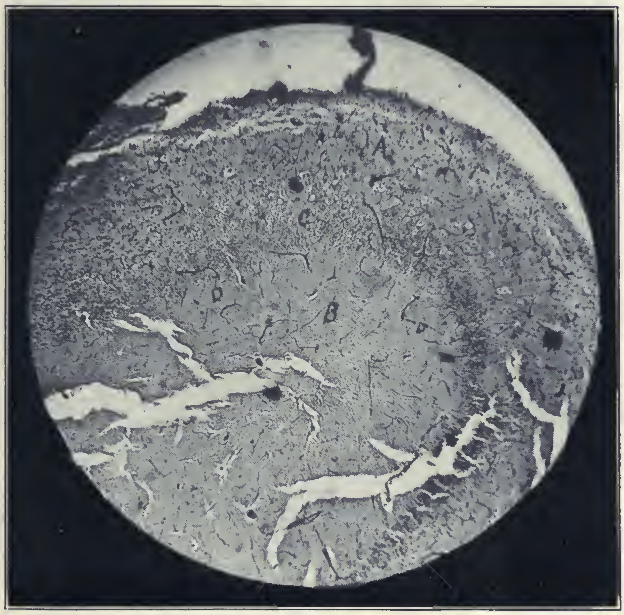

Fig. 28.—Brain cortex, low power, showing extreme vascular congestion with little or no change of the parenchyma. All layers, molecular, of pyramidal cells and polymorphous cells show no particular changes or involvement.

COMPARISON OF CONCLUSIONS

We quote *in extenso* the conclusions of Kolmer and Lucke concerning the organs of animals treated with mercury, by all methods except one—inhalation, in order that the summary of their results may be conveniently compared with our own findings in the organs of animals treated by inhalation.

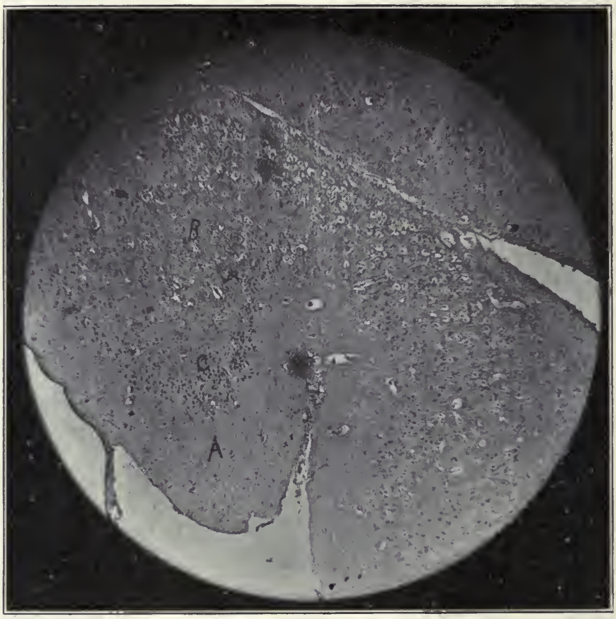

Fig. 29.—Brain, high power, showing the extreme capillary congestion and filling of larger blood vessels, *A*, with agglutinated and otherwise changed red cells. The nerve cells are free from degenerative changes.

"1. The administration to rabbits of different soluble and insoluble mercurial compounds commonly employed in the treatment of syphilis by intramuscular and intravenous injection, inunction and oral administration, and in amounts analogous to the maximum dose given to human beings, results in the production of tissue changes in all organs examined, namely, the brain, heart, lungs, spleen, liver and kidneys.

"2. The most conspicuous changes were found in the brain, in the nature of perivascular round cell infiltrations, and in the kidneys as tubular and capsular glomerulonephroses of varying degree of severity. Details of the histologic changes in these and the other organs included in the study are described.

"3. The degree of tissue injury caused by the different preparations of mercury appears to bear a direct relation to the actual amount of pure mercury absorbed irrespective of the kind of preparation and route of administration."

Between the results observed by Kolmer and Lucke in the organs of animals treated by every kind of mercury and every method of administration except inhalation, and our findings in the same organs after death following inhalation of mercury vapors, no essential differences are evident. Indeed, the histologic appearances in both instances are very much alike. The sections from all organs, judging from *their* illustrations and descriptions, a few of which are reproduced, are so similar to ours, that one is justified in concluding that *the effects of mercury upon the organism, no matter how introduced or absorbed, are the same.* The differences are of minor importance and some are probably the result of

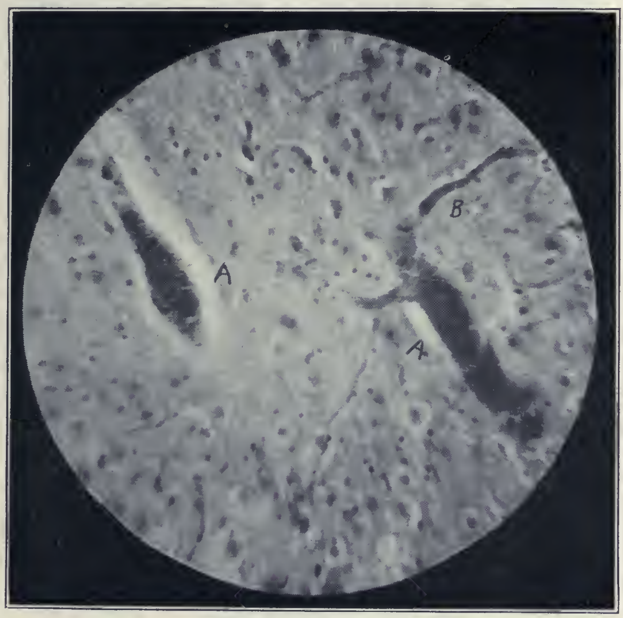

Fig. 30.—Brain cortex, low power. Experiment 18. Also shows no marked changes.

individual peculiarities in the laboratory animals. Our experience corroborates the statement of Kolmer and Lucke that—"As expected, individual animals exhibited varying degrees of tissue injury, so that a comparison of the kind and severity of the lesions produced by the different preparations of mercury administered by different routes, in multiple small doses, is possible only in a broad and general manner."

Comparing the studies of individual organs made by these workers and by myself, we find that: Of the *brain and meninges* they state that "These tissues showed an interesting and unexpected perivascular round cell infiltration; curiously this change is regarded as more or less constant in syphilitic infection of these tissues, and their findings quite naturally raise the question of the significance of perivascular round cell infiltration in the brain of syphilitic subjects who have taken mercury during life. At the present time

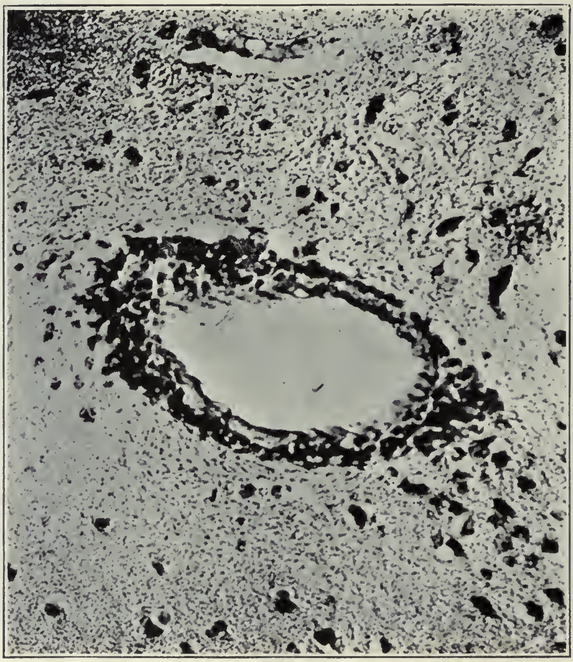

Fig. 30*a*.—Rabbit; eight intramuscular injections with mercurial oil (gray oil). Brain: Perivascular round cell infiltration. The perivascular jacket consists of several layers of small and large round cells. Many of the vessels possessed such jackets. (Kolmer and Lucke.)

we are continuing our investigations with monkeys, in order to shed further light on this and other interesting histologic changes due to the administration of mercurial compounds.

"Among the animals receiving a large amount of mercury, some congestion and edema with slight perivascular round cell infiltration were noted in the pia mater. These lesions were somewhat more marked in animals which received intramuscular injections."

One of the principal facts observed by Kolmer and Lucke in connection with the central nervous system, is as may be seen from the above, a perivascular round cell infiltration. This, however, they detected only in some of the sections, and at times they were unable to distinguish whether the extraordinary accumulations of round cells were independent infiltrations, perivascular jackets or were within the vessel lumen. We were seldom able to observe lymphocytic infiltration; there were no striking accumulations of small cells either in the cerebrum, cerebellum or spinal cord, and only occasionally did we observe a tendency in that direction among the animals that lived longest. The prominent feature of our cerebrospinal specimens was the marked congestion of blood vessels, thrombi and conglutinated red cells. No changes were observed in the ganglion cells; no necrotic areas, no endothelial cell proliferation was evident. Perhaps our animals succumbed too rapidly to permit the constructive and protective formation of leucocytic infiltration which took place in their long-lived animals.

The *esophagus* and *the small and large intestines* were not studied by these authors and therefore no comparison can be made.

Of the *heart* they say in their summary: "As a general rule this organ showed no changes, although among those animals receiving the maximum amount of mercury there were evidences of slight focal necrosis of the muscle cells with intramuscular round cell infiltration. Occasionally the capillaries contained masses of conglutinated and hyalinized erythrocytes." These findings do not materially differ from ours. Focal necrosis, which they also observed in one of the brain specimens, we did not detect; otherwise our findings fully coincide with theirs, even to the slight perivascular cellular infiltration, as shown in one of our illustrations.

Concerning the *liver, spleen and adrenals,* their summary of the conditions found in nowise differs from ours in any essential. Our observations agree substantially with their findings, which they describe as follows:

Spleen.—"The changes found in this organ consisted mainly of hyperemia, and hemosiderosis, apparently due to increased blood destruction as the result of the administration of the different preparations of mercury.

Liver.—"Changes in the liver were usually inconspicuous, and when noted at all, comprised congestion, filling of the sinusoids with partially hemolyzed erythrocytes and hemosiderin staining of neighboring hepatic cells."

As to the kidneys, however, some differences apparently exist in our findings. While all other factors, such as cloudy swelling, fatty degeneration, extensive hyperemia, localized necrosis, exudates and casts were observed by both of us, calcareous infiltrations, or very marked lymphocytic accumulations were absent in our sections. Otherwise we can subscribe fully to the description of this organ which is given by these investigators: "These organs have shown the most conspicuous changes analogous to those previously described and every one shows some degree of tissue injury, the severity varying considerably according to the amount of mercury administered.

"The most constant lesions were found in the tubules, characterized by cloudy swelling fatty degeneration, frank necrosis, calcareous infiltration and the presence of large numbers of casts. The convoluted tubules suffered most; the limbs and loops of Henle were sometimes involved, while the collecting tubules generally escaped.

"The glomeruli were sometimes hyperemic, and among animals receiving the larger amount of mercury, granular exudates occurred in the capsular spaces. Among the animals surviving for the longer periods of time, there were evidences of repair of the tubular cells accompanied by interstitial changes of lymphocytic infiltration and fibrosis."

Of the *lungs* Kolmer and Lucke speak as follows: "Changes in the lungs, when found at all, mainly consisted of congestion and slight edema. It was of considerable interest to find that the erythrocytes were frequently conglutinated and hyalinized, resembling the changes found in the lungs of rabbits after the administration of arsphenamine." As may be seen from the above only very minor injuries were found by these investigators in the lungs.

Our findings agreed with theirs only in cases where the animals were subjected either to mercury vapors very much diluted with air, or to more concentrated vapors administered at longer intervals and for short periods, whereas in the animals subjected to more concentrated vapors of mercury, or where its administration was frequent and more prolonged, i.e., where the mercury vapor was crowded, the changes in the lungs were profound. Here, marked bronchitis, frequent hemorrhagic areas, infarcts, areas of infiltration, collapse and other serious changes were encountered.

CONCLUSIONS

1. Experiments are presented in which the symptomatology and the gross and microscopic pathologic changes in the organs of animals (guinea pigs and rabbits) subjected to inhalations of mercurial vapors are described.

2. A comparison is made between the effects of mercury when it is administered by inhalation and the effects of oral, hypodermic and inunction methods as described by Kolmer and Lucke.

3. It was found that under like circumstances, the pathological changes following the administration of mercury, in whatever form and by whatever route, are approximately identical.

4. It was found that the toxic changes following mercurial inhalations consist of marked congestion of many organs, severe destructive processes affecting the intestinal tract and kidneys and lesser injuries to the liver, spleen, adrenals and nervous system.

5. It may also be stated that the effect of mercurial vapors upon the respiratory system depends upon their concentration and the manner of their administration. Strenuous inhalations of concentrated vapors induce serious pathologic lesions. Diluted vapors, smaller and less frequent dosage are not productive of harmful effects in the lungs.

I am greatly indebted to Dr. E. C. Schirmer for most valuable assistance in the preparation and interpretation of pathologic specimens and to Drs. Kolmer and Lucke for the privilege of reproducing some of their original microphotographs. I wish to thank them for their very kind cooperation.

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[3] Abel: Histoire Therapeutique du Mercure et de ses Composes, Paris Thèsis, 1910. Quoted by Pillot.

[4] Darrien: Syphilis et Mercure, Paris, 1905.

[5] Ricker and Hesse: Arch. of Path. Anat., 1914.

[6] Ibid.

[7] Kolmer and Lucke: Arch. Dermat. and Syphil., 1918.

SYPHILITIC GENITAL CHANCRE*

By Mihran B. Parounagian, M.D., and Herman Goodman, B.S., M.D., New York City

(Received for publication, June 8, 1922)

A REVIEW of the majority of text books and monographs on syphilis gives the impression that the genital syphilitic primary lesion or chancre can be more or less easily classified, named, and pigeon-holed according to one or another character which is regarded as essentially pathognomonic and of great value. Some of these differential characters bear the mark of extreme age, and if one will, can be traced back to points of origin early in clinical syphilology when the chancre was distinguished from the chancroid by reason of being followed by secondary generalized symptoms. Needless to say, most of the characters used are not infallible, and many "soft" sores harbor the Spirochete pallida of syphilis; many lesions which are multiple are syphilitic chancres; and induration may be the result of ill-advised self-treatment with caustics. On the other hand, the diagnostic demonstration of Spirochete pallida is not always possible, nor always successful in primary syphilis. The Wassermann reaction is regularly negative early in the chancre stage of syphilis. Repeated dark-field examinations and repeated Wassermann tests should always be made. In no case, however, should clinical observation be disregarded. Despite the fact that it is not possible to prepare a single standard chancre by which all examples are to be judged, one should not overlook the possibility of chancre in lesions, especially of the genitals, and proper measures taken to insure certain diagnosis.

The clinician may readily recognize the chancre of syphilis but under certain circumstances, even a genital lesion may give no hint as to its syphilitic nature. Often the mature observer who has had many opportunities of studying penile lesions may not be certain clinically, and requires the aid of the cooperating workers in microscopy and serology. The possibility of syphilis should thus be reserved, and a favorable immediate prognosis held in abeyance until the exact nature of the lesion is determined.

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*Illustrated by photographs from the Collections of Parounagian and Goodman.

A number of photographs were selected for publication with an idea of utility in emphasizing how impossible it actually is to portray "the chancre" of syphilis. A chancre may be of any type, and may simulate nonsyphilitic lesions. With time, the chancre changes and local applications may also alter its appearance, but even the chancre which has not been tampered with presents itself in a multitude of forms. It is idle to name these, and for the present we must content ourselves with their photographic reproduction.

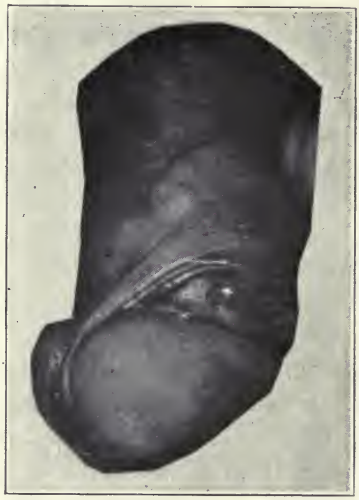


Fig. 1.—Primary syphilis: pinhead-sized circumscribed ulceration of the mucous surface of prepuce said to be of ten days' duration.

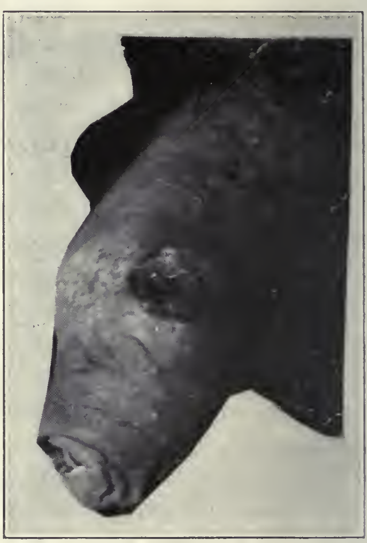


Fig. 2.—Primary syphilis: chancre was perfectly round, circumscribed, ulcerated in center and with advancing rim.

Although vesicular chancres are extremely rare, it has been our good fortune to examine two such lesions. The first one had been diagnosed as "herpes progenitalis" and such a diagnosis certainly seemed the proper one. The dark-field examination was done, however, and the number of Spirochete pallida present was very large. In this instance he had ruptured the vesicle. In the second patient, one of the associates had seen a single vesicular lesion on the penis of a patient passing through the genitourinary department, and advised a dark-field. When seen the next day, the vesicle was ruptured but the resulting small ulcerating depression was teeming with spirochetes of the pallida type. Unfortunately, these cases were seen before our trials in photography, and there has been no film record. The first photograph (Fig. 1) shows a pin-head sized circumscribed ulceration on the mucous surface of the prepuce. According to the patient it had been present to his knowledge not more than two days. Both this information, and any statements regarding possible incubation time are not considered as highly important from most clinic patients who are not good observers, and are exposing them-

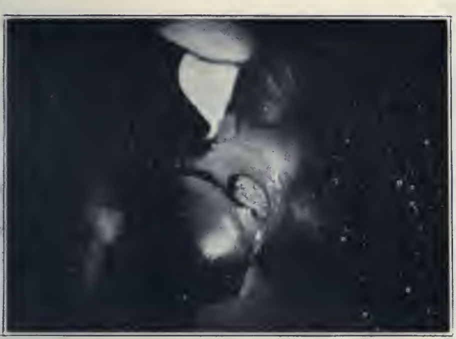


Fig. 3.—Primary syphilis: chancre of the mucous surface of the prepuce.

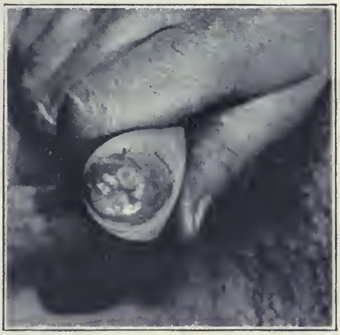


Fig. 4.—Primary syphilis: chancre within phimotic prepuce.

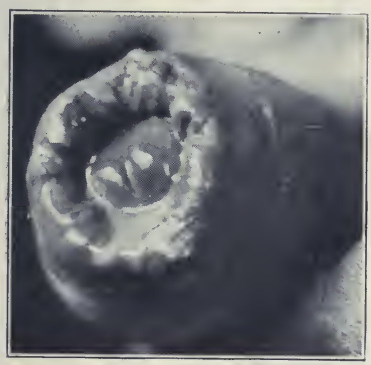


Fig. 5.—Primary syphilis: rosette chancre.

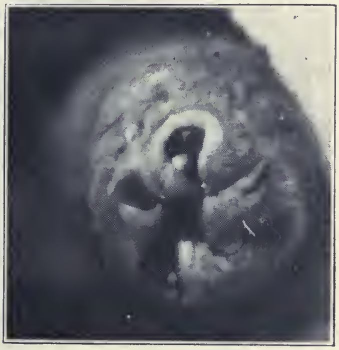


Fig. 6.—Primary syphilis: rosette chancre.

selves at very short intervals. To suggest that this small lesion was an ulcerated herpes would be a little far fetched as for the most part, herpetic eruptions of the genitals present multiple vesicles, although it is possible that even with an eruption of herpes, one of the lesions may be the site of a syphilitic chancre. The demonstration of pallida in smears from this lesion, and the immediate effect of appropriate treatment made the diagnosis absolute.

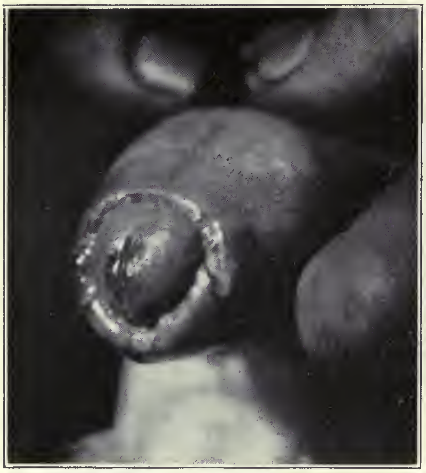


Fig. 7.—Primary syphilis: rosette chancre.

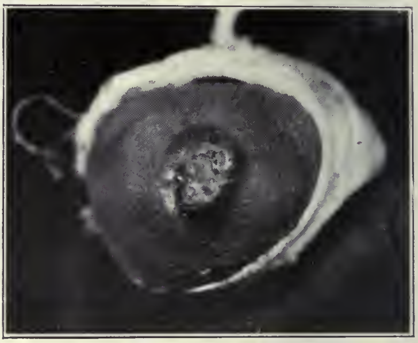


Fig. 8.—Primary syphilis: chancre of the urinary meatus.

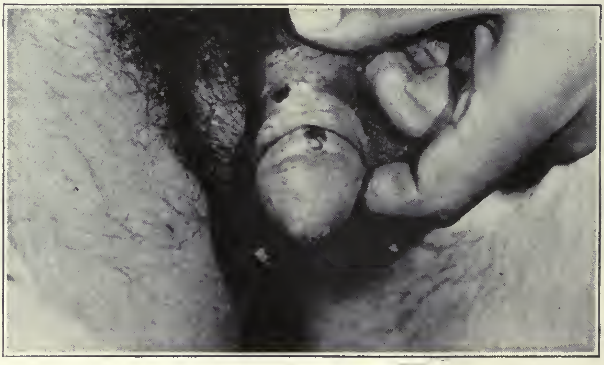


Fig. 9.—Primary syphilis: multiple chancres.

The second chancre pictured (Fig. 2) is somewhat larger than the first, perfectly rounded and circumscribed, with a definite advancing circle and an ulcerating center. The rim is particularly important, and many times if searches for Spirocheta pallida are reported negative, it means that this rim has not been the area from which the smears were taken. This chancre was less than ten days old, and there had been no satellite gland enlargement.

Fig. 3 is one of a chancre of the mucous surface of the prepuce which shows a polycyclic circumference, and a tendency to be hypertrophic rather than ulcerative. The circumscribed raised edge is sharply marginated from the mucous surface of the prepuce, but the ulcerated center is hardly depressed. When the prepuce is rolled back or forth in such a case, the chancre does not fold over, but passes across from the exterior to the interior as a button of a coat passes through the buttonhole. This is an important sign of induration, and needs hardly to be corroborated by digital examination.

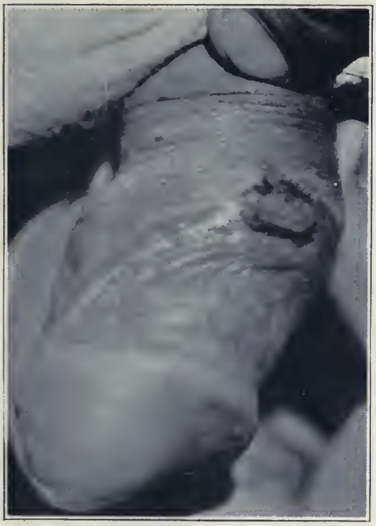


Fig. 10.—Primary syphilis: chancre of the mucous surface of prepuce.

Although "Syphilis d'emblee" is a recognized possibility, one would not call the patient in Fig. 4 an example, for the chancre although hidden in one sense of the word is undoubtedly located within the phimotic prepuce, either on the surface of the glans or on the mucous surface of the prepuce. The tumor can readily be seen and even more readily felt through the prepuce. Acquired phimosis of this character is always suspicious, and if attended with palpable tumor and a discharge, syphilis should certainly be thought of as a possibility. The search for spirochetes is especially interesting because of the abundance of contaminating possibilities, as S. refringens, and the spiral organism of genital Vincent's disease, or the Fourth Venereal Disease. The glands of the groin may enlarge and prove a valuable aid.

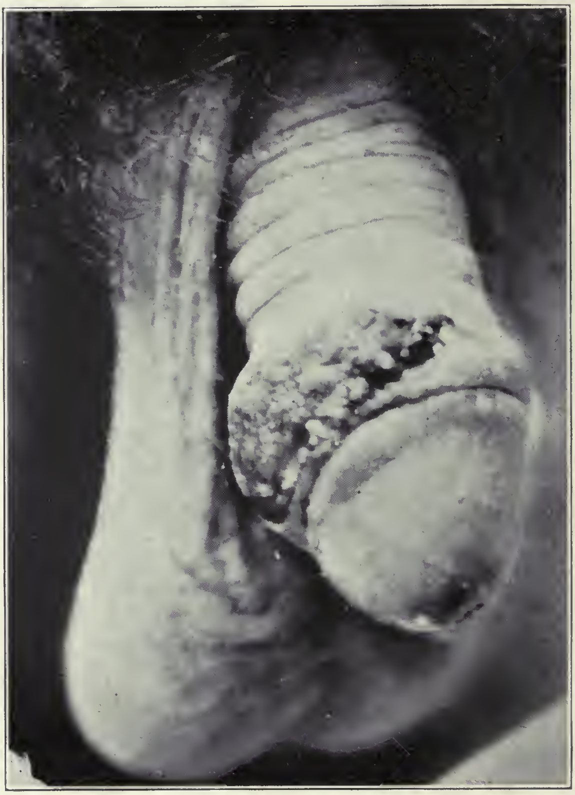


Fig. 11.—Primary syphilis: large chancre of mucous surface of prepuce.

The next series of photographs (Figs. 5, 6, 7) serve to illustrate a type of syphilitic chancre which has not been emphasized, namely, the rosette chancre. It can obviously occur only in those with a

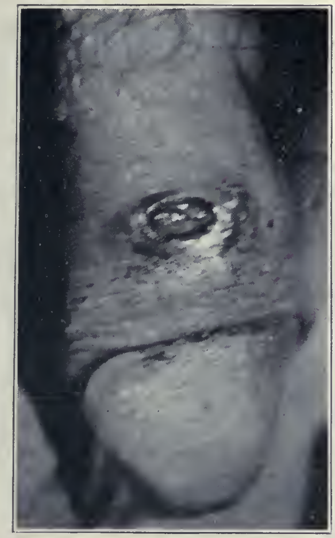


Fig. 12.—Primary syphilis: chancre of the skin surface of prepuce.

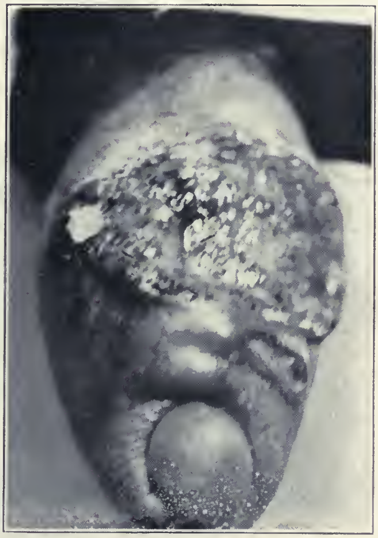


Fig. 13.—Primary syphilis: large chancre of skin surface of prepuce.

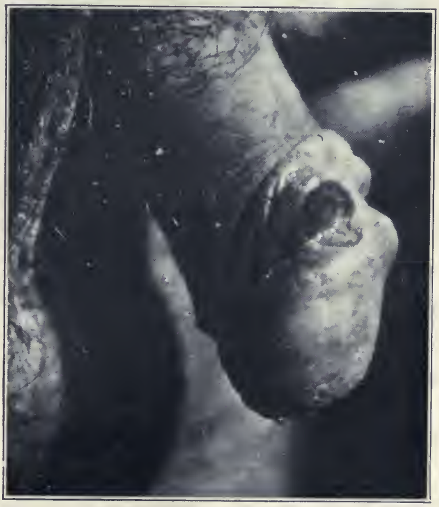


Fig. 14.—Primary syphilis: chancre of coronal sulcus.

prepuce. The number of lesions may vary from 5 to 20. Each is probably a separate chancre, but by reason of the anatomy of the part they share about equally in the resultant clinical appearance. The edema and induration are typical. There may be a concomitant phimosis, but never as marked in the phimosis of concealed chancre of the type previously described. At times, there may be an abundant purulent discharge which may be mistaken for the discharge of an accompanying urethritis, or the uninitiated may consider the entire process one due to the gonococcus, and miss the

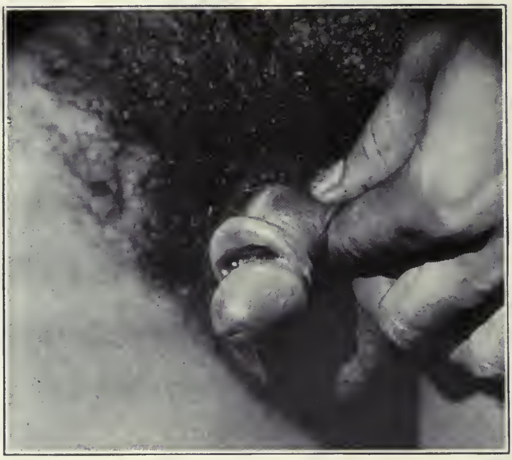


Fig. 15.—Primary syphilis: chancre of sulcus with much induration.

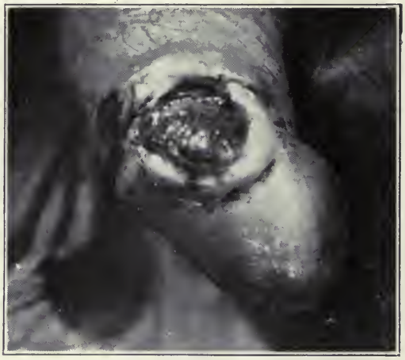


Fig. 16.—Primary syphilis: chancre of the sulcus with more involvement of glans than of prepuce.

significance of the manifestations of early syphilis. The last of this series illustrated (Fig. 7) again shows the induration as an attempt to draw back the prepuce is attended by stretching and only a part of the glans can be exposed.

Chancre of the urinary meatus (Fig. 8) may be on either one or the other lip, or more often on both. The lesion when it first appears may be very insignificant. In a very short time, ulceration as pictured appears, and the possibility of chancre is more readily appreciated.

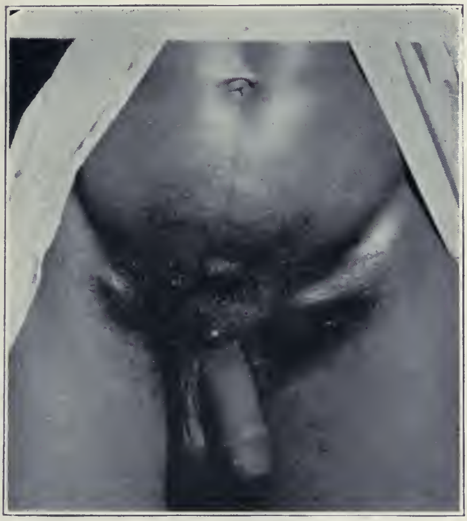


Fig. 17.—Primary syphilis: pubic chancre and bilateral inguinal adenopathy.

Although in the main, syphilitic chancres are single, multiple syphilitic chancres are not uncommon. Fig. 9 shows a chancre of the glans and one of the mucous surface of the prepuce. We have also seen syphilitic chancres numbering 4 in one patient, two on the penis, and two on the lips. It is very important in the bacteriologic examination to prepare smears from each of the lesions and not be satisfied that a negative from one means that the others are also negative.

The mucous surface of the prepuce being easily traumatized is all too often the site of syphilitic chancre (Fig. 10). The larger (Fig. 11) compares favorably with one type of text book chancre, but the earlier illustrations should have shown by now how fallacious it would be to depend on this type for clinical diagnosis.

The skin surface of the prepuce is not immune to syphilitic infection, and two further examples of chancre at this location are pictured. The ulceration of the smaller one (Fig. 12) could hardly be mistaken for any other condition, and certainly the larger one (Fig. 13) could easily have been diagnosed from its appearance alone.

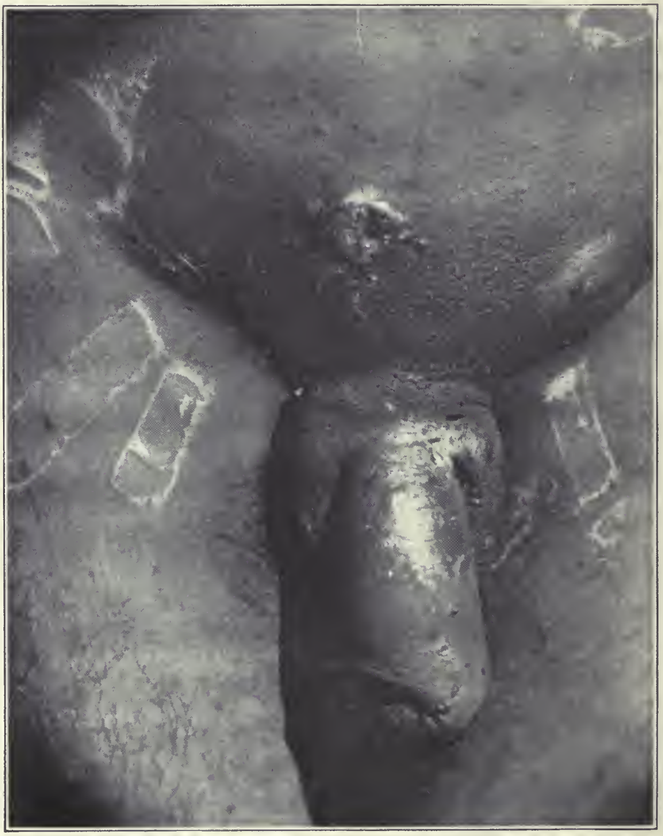


Fig. 18.—Primary syphilis: chancre of pubic region and incised gland of groin with secondary syphilitic lesions of penis and abdomen.

The sulcus is also a favorable place for syphilitic chancre and those illustrated are good examples. The smallest (Fig. 14) most sharply cut one shows coaptation: one half of the lesion on the glans, the other half on the mucous surface of the prepuce. Such an arrangement should not be taken as evidence of autoinoculation and the diagnosis of chancroid made. Such a procedure would not take into account the evident sclerosis, the sharpness of the margin, the advancing rim, and other findings, as dark-field. The induration in the next chancre (Fig. 15) of the sulcus needed no palpation. One edge actually stood up, and the analogy to the buttonholing would have been borne out in passing the foreskin down. As shown in the next picture (Fig. 16) the chancre need not advance equally on the glans and on the mucous surface of the prepuce. In this figure there is greater involvement of the glans, with relatively little of the prepuce.

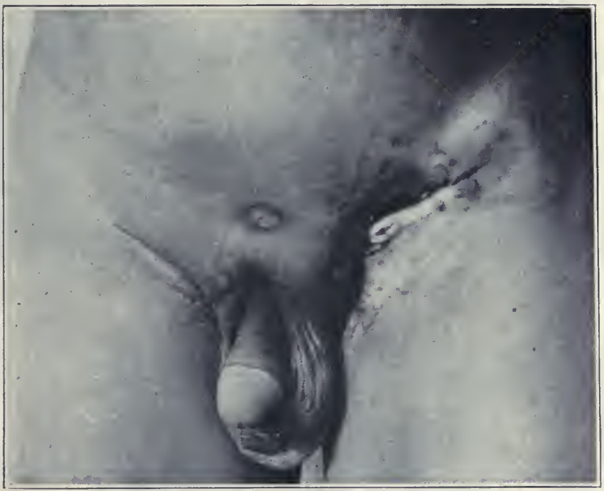


Fig. 19.—Scar of chancre of pubic region with recent bubo from chancroid infection.

The pubic region may be the site of syphilitic chancre, and the three (Figs. 17, 18, 19) pictures presented are chosen to show the type of lesion and the associated bilateral adenopathy. In the colored patient (Fig. 18) the lesions of the secondary stage may be noted on the penis and on the abdomen. The glands had been incised in this man at another clinic on the mistaken diagnosis of chancroidal bubo. The scar of the pubic chancre in the third case

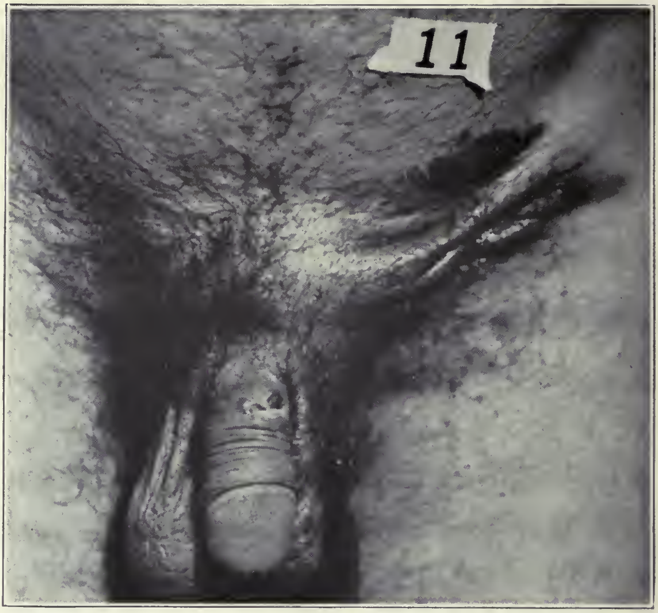


Fig. 20.—Chancroid with bubo.

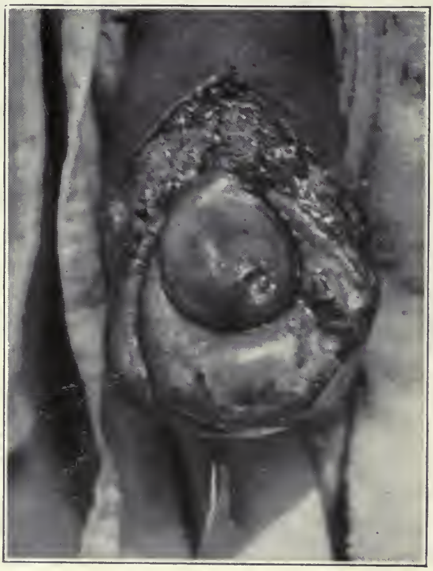


Fig. 21.—Dorsal slit from chancroid within preputial cavity.

(Fig. 19) is really typical, and this Chinaman had a more recent chancroidal infection with the resulting bubo as shown.

For comparison, a chancroidal lesion is pictured with the bubo. The last picture is that of a dorsal slit to expose for treatment a lesion within the preputial cavity not otherwise accessible.

The method of choice for the diagnostic demonstration of Spirocheta pallida is by dark-field illumination. The requisites for the utilization of this method are: the dark-field apparatus, microscope with oil immersion and the essential ''funnel stop'' source of light, slides, cover slips, and immersion oil.

We were fortunate also in having the opportunity of supplying material for the bacterial diagnostic procedures revived by Teague. and although the method is one which is entirely desirable, the possibility of ignoring syphilitic infection by reason of the proof of chancroidal infection has always appeared a danger. Should treatment of a sore for chancroid be instituted (before any Spirocheta pallida were demonstrated) on the laboratory report of positive Ducrey organisms, further search for spirochetes would be rendered impossible and no means taken to combat the associated syphilis until later symptoms of the diseases appeared. Hence for the present at least we are more satisfied to temporarily postpone treatment of a sore apparently of nonsyphilitic nature than to treat such a lesion and miss a syphilitic infection until the secondary eruption.

The abuse of antiseptics either self applied or on the recommendation of the drug store clerk makes the demonstration of spirochetes difficult at times, and gland puncture may be necessary. If possible other methods of diagnosis should be utilized, and diagnosis by confrontation of the older writers may well be practiced. Clinical observation on the basis of large experience in the correlation of the appearance of the sore, the bacterial findings, the clinical course of the case, and the results of antisyphilitic treatment will remain one method of diagnosis not easily displaced.

Note: The lesion of the frenum has purposely been omitted from this paper as it will form the basis of a separate communication.

VENEREAL DISEASE CLINIC. THE TOLEDO MUNICIPAL HOSPITAL

By Earl W. Huffer, M.D., Toledo, Ohio

(Received for publication, July 17, 1922)

EVERY public institution should justify its existence, but in the case of Public Health Organizations a two-fold obligation is imposed. The first is due the tax-payers on whom the burden of financing must fall. They have the right to know that their funds are being expended, not only in a worthy cause, but in one that can show results. The second duty is to the medical profession of the community, whose privilege it is to feel that their interests are being safeguarded, that no attempt is being made toward socializing medicine and that no spirit of competition surrounds the activities of the organization.

There is current opinion to the effect that the medical profession is, and has been, considerably exploited. Medical men feel that too many agencies are proffering free or near-free medical service to the detriment of the regularly licensed practitioner. This accusation is no doubt true in many instances, but so far as the Toledo Municipal Hospital Clinic is concerned, it is the desire to cooperate and collaborate with the private physician at all times.

The problem of venereal control, however, presents difficulties that do not attend most of the other ills affecting human kind. If these diseases are to be controlled, the patient must be made noninfectious. It is a costly process to achieve this in private practice and unless it is accomplished little has been gained. There may be abundant grounds for argument over the relative merits of various methods of treatment, but there can be no controversy where the criteria of ''cure'' or ''arrest'' of venereal diseases are concerned. It is this aspect of the venereal problem, too, that is of prime importance. It is in this phase of the fight against venereal disease that the Venereal Dispensary is well nigh indispensable, because it affords opportunity for sufficient treatment to those who want it but cannot afford it, and it compels the reluctant one to see it through.

During the late war, at the suggestion of the U. S. P. H. S. the City of Toledo established a clinic for the control of venereal diseases. The Clinic had its inception as a war-time emergency measure, but, as it met a long-felt need, it has continued and expanded.

The premise from which the present Municipal Hospital Clinic operates is that of a police power. In 1920 the Legislature of Ohio enacted a code of Health Laws. The communicable diseases were all made reportable and quarantine was authorized for their control. The venereal diseases, quite naturally, fall within this classification, and here in Toledo have been treated as such. The Venereal Control Clinic has made energetic efforts to carry out the object of the laws in this respect, namely, to prevent the spread of venereal diseases.

Fig. 1.—Venereal Clinic, Municipal Hospital, Toledo, O.

Laws are enacted, of course, not for the conscientious, law-abiding citizen, but for him whose sense of responsibility is slight or even wanting. It is with this latter class of patients we are mostly concerned, although we do not wish to depreciate the humanitarian aspect of dispensary work at all. We do, however, stress the police power as delegated to us by the State Health Laws.

ORGANIZATION

The Toledo Municipal Hospital Clinic is, in our opinion, a unique institution being, as it is, a strictly municipal undertaking controlled by the City of Toledo and depending, as it does, upon the cooperation of the Council, the Mayor and his Cabinet, the Police Department, the Health Division and the personnel of the Clinic itself. It is an activity under the control of the Welfare Department and is supported by the budget of that branch of the City Government. It bears no relation to the State Health Department or U. S. P. H. S. other than to render reports monthly to those

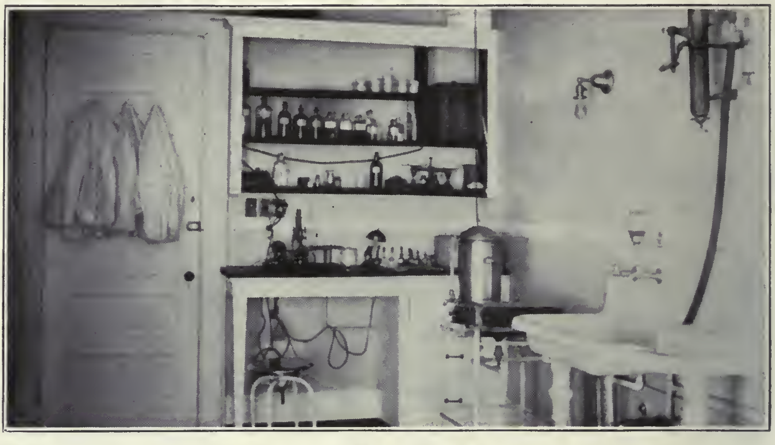


Fig. 2.—Small laboratory in male clinic.

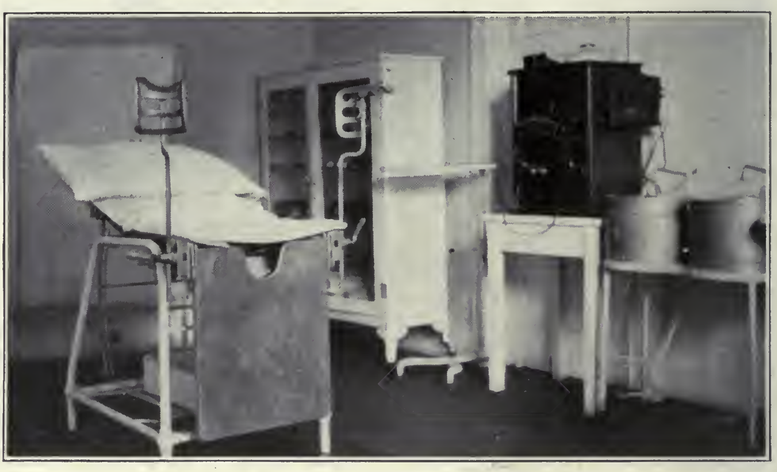


Fig. 3.—Endoscopy and Cystoscopy.

bodies. The policies of the Clinic are, therefore, entirely controlled by the City Government.

The Clinic is in charge of a Director, who is responsible for all departments of which there are three, Urological, Nursing and Clerical.

The Urological Staff consists of the Director who is Chief Urologist, consultant and advisor in all cases, the Assistant Director who has charge of the female service, and two assistant urologists. Three of the Staff have practices limited to urology, but all receive a small salary for their services in the Clinic.

The Nursing Staff is composed of the Head Nurse who is also the Superintendent of Hospital, eight full-time, graduate nurses and two male nurses. They assist with the treatments, at operations and attend the ward cases.

The Clerical Force includes a full-time social worker, a stenographer and a statistical clerk. The social worker investigates all applicants, makes personal visits and handles the follow-up work. The statistical clerk keeps all records, makes the necessary reports, collects fees from those who can afford to pay a little for their treatment and acts as bookkeeper.

THE CLINIC

The names "Municipal Hospital" and "Municipal Clinic" are sometimes used interchangeably. The institution, as before stated, began as an emergency organization for venereal control during the war. It has since expanded and included in its scope of activities contagious disease other than venereal. But the Venereal Control Clinic is still the real *raison d'être* of the plant and it is that part with which this paper is wholly concerned.

The Municipal Hospital Clinic occupies a two-storied brick building in the down-town district. It is easily accessible to patients, yet not conspicuous.

The ground floor is occupied by the executive offices, men's waiting room, the clinic for men, a small instrumental room and a small, inadequate operating room. There are two large wards on this floor, one for men and one for women, but they are widely separated and intermingling is not possible. Thirty-eight beds are available in the hospital and the overflow on the female side is accommodated at the Detention Home.

The second floor is devoted to the clinic for women. There is a large central waiting-room around which are grouped smaller rooms, one of which is used for treatment purposes and the others as small wards where the more acutely ill patients and young girls who must be confined can be kept and separated from the prostitutes.

Fig. 4.—Woman's treatment room.

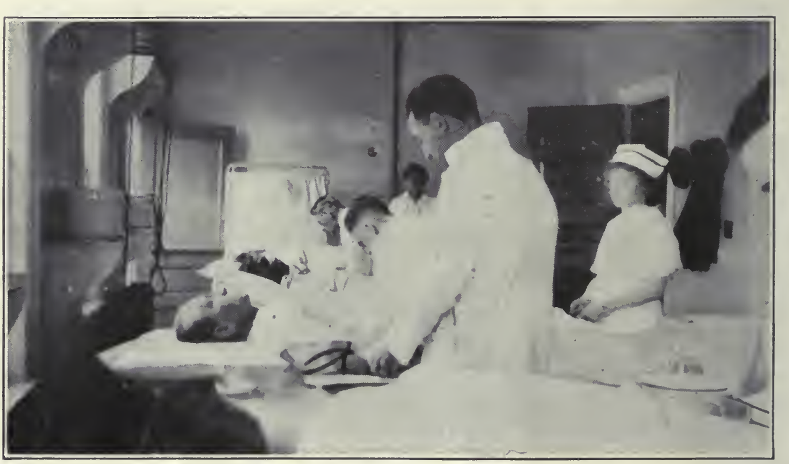


Fig. 5.—Arsphenamine day.

The present location has met fairly well the demands thrown upon it, but the addition of other contagious diseases with the ever-increasing attendance in the venereal clinic itself makes expansion almost imperative. We are handicapped by a lack of operating facilities, making it necessary for us to lose contact with operative cases by referring them to other hospitals. It is also desired to confine all police charges to the hospital and obviate the present system of daily transporting them from the Detention Home. There is considerable enthusiasm for a new Municipal Hospital, and this, if plans carry through, will give us all that we now lack. Since this paper was written the City has purchased a new Municipal Hospital Building which, when properly remodeled, will fulfill all our wants. It will be ready for occupancy about January first.

SOURCES FROM WHICH PATIENTS ARE DERIVED

The channels through which our patients come to us are many and varied. For convenience and easier understanding we will group them into two classes.

I. Prostitutes.
II. Others.

I. *Prostitutes.*—Licensed prostitution is, of course, prohibited and segregated districts are no more, but this fact does not disprove the existence of promiscuous and illegal sex relations. So long as there are men with money and women willing to exchange virtue in the open marts this exchange will likely continue. We do not believe Toledo to have been any worse than other cities of similar size, but here there is, and has been, an active effort to curb, not so much prostitution *per se* as its harmful effects, the dissemination of venereal disease.

In handling prostitutes the Clinic cooperates with the Police Department and with the Sanitary Police of the Division of Health. The Police Department maintains a special detail known as the "Vice Squad" one of whose chief duties is the apprehension of women engaged in commercialized vice. These women are arrested on suspicion and remanded to the station or the Detention Home where they are held "for Municipal Hospital." During the open hours of the Clinic, they are transported to the hospital for examination. If as a result of the examination, they are found to be infectious they are at once quarantined and detained, either in the hospital or in the Detention Home if no beds are available in the hospital. These cases are confined for the full period of their infectiousness.

II. *Others.*—The channels through which cases other than the police charges come to us are many. Other hospitals having no facilities for the care of venereal disease send such cases to us. Charitable institutions, such as the District Nurses, the Thalian Tuberculosis Dispensary, Homes for Girls, etc., refer many. The Public School Nurses and outside physicians also refer indigent patients to us. Some of the cases have been reported directly to the Health Division and are brought in by the Sanitary Police. These latter cases are sometimes reported by employers, others are reported "for spite," this being particularly true amongst the foreign population. But by far the greater number of patients are voluntary applicants, especially the male patients. Those who can pay outside physicians are at once told to seek medical advice outside and an effort is made to direct them along the proper channels; others are accepted.

METHOD OF HANDLING PATIENTS

The Clinic is open every day except Sunday, and three nights a week for men only.

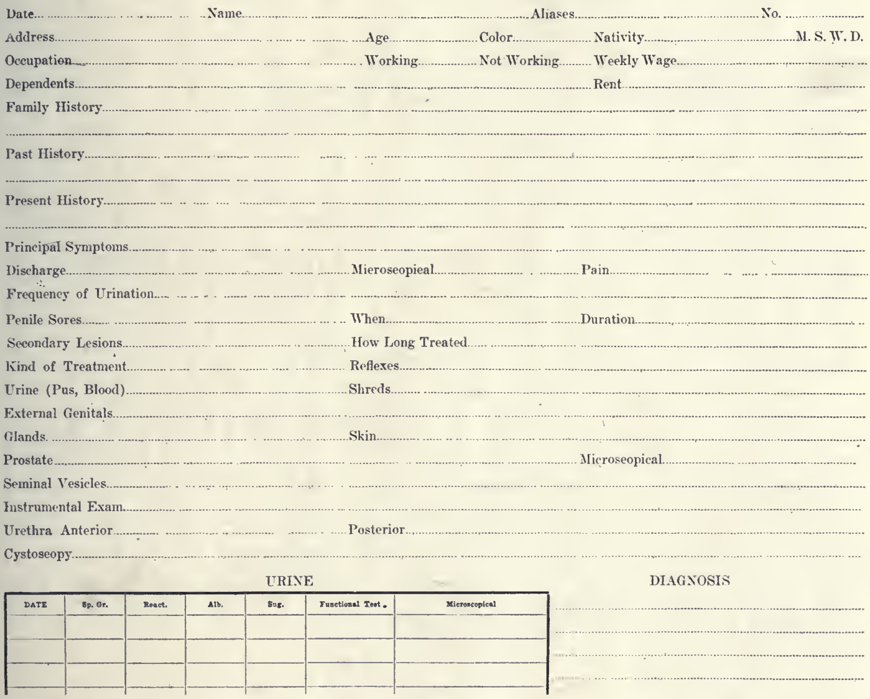
Hours in the Clinic for Women: Daily 9:30 A.M. to 11:00 A.M. except Wednesday and Sunday.

Hours for the Male Clinic: Daily 9:30 A.M. to 11:00 A.M. except Wednesday and Sunday; from 6 to 7 P.M. Monday, Wednesday and Friday.

On Wednesday from 9:30 to 11:00 A.M. the entire staff is devoted to the administration of intravenous treatments. No new cases are admitted on this morning.

When the new case first applies, from whatever source he comes, he is directed at once into the office of the Social Worker. A thorough social history is developed. If the applicant is considered a Clinic case, the social history is filled in on the Clinical record and the patient with his card sent to the statistical clerk. The latter enters the patient's name in the "Day Book," keeps the card and directs the patient to the waiting room until the physician is ready for him.

The physician collects the cards from the desk of the statistical clerk, taking the old cases first. When he is ready the doctor summons the new patient into the examining room where the history is taken and urological examination is made. When the diagnosis has been made the patient is advised concerning his trouble and treatment instituted. The diagnosis is recorded on the front of the card, and on the reverse the physician indicates just what was done for the patient. (This will be explained later under "Records.") This data is later copied in the "Day Book" opposite the patient's name and the charge posted against him.



Date ...... Name ...... Aliases ...... No. ......
Address ...... Age ...... Color ...... Nativity ...... M. S. W. D.
Occupation ...... Working ...... Not Working ...... Weekly Wage ......
Dependents ...... Rent ......
Family History ......
Past History ......
Present History ......
Principal Symptoms ......
Discharge ...... Microscopical ...... Pain ......
Frequency of Urination ......
Penile Sores ...... When ...... Duration ......
Secondary Lesions ...... How Long Treated ......
Kind of Treatment ...... Reflexes ......
Urine (Pus, Blood) ...... Shreds ......
External Genitals ......
Glands ...... Skin ......
Prostate ...... Microscopical ......
Seminal Vesicles ......
Instrumental Exam ......
Urethra Anterior ...... Posterior ......
Cystoscopy ......

URINE

DATE	Sp. Gr.	React.	Alb.	Sug.	Functional Test.	Microscopical

DIAGNOSIS

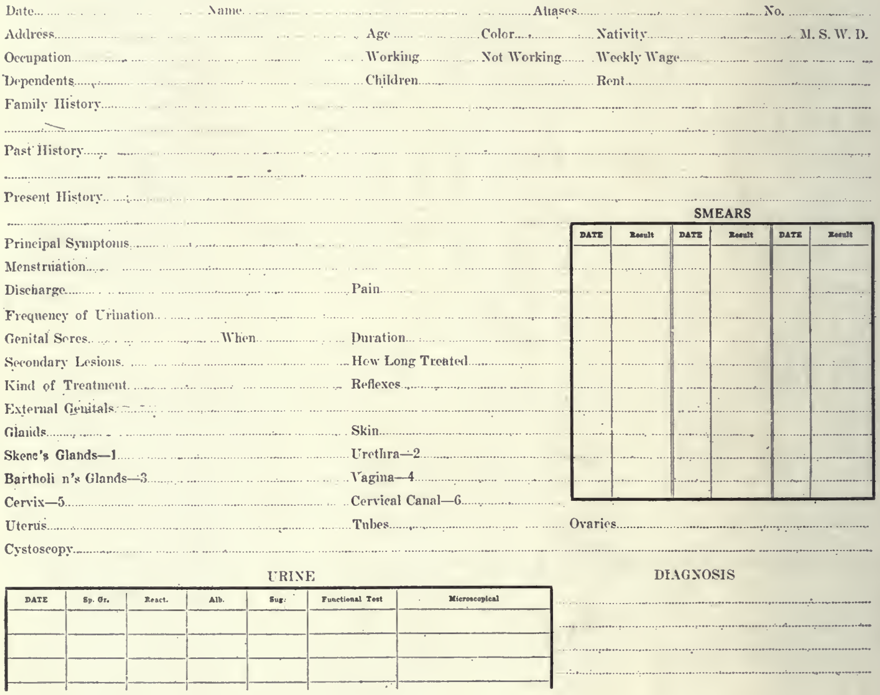
Fig. 6.—Original chart, white.

On his subsequent visits the patient goes directly to the statistical clerk and gives his name. His card is removed from the file, the name entered in the "Day Book" and the patient passes on into the waiting room.

In addition to the complete history and thorough examination all patients have a Wassermann done routinely. In case the blood findings and the clinical history are at variance both are checked. With prostitutes much reliance has to be put in the blood findings and with them a Wassermann is routine every three months as are smears every week.

HISTORIES AND RECORDS

The attempt has been made, so far as paper work is concerned, to simplify wherever possible and to prevent duplication of records.



Date.......... Name.......... Aliases.......... No. ....
Address.......... Age.......... Color.......... Nativity.......... M. S. W. D.
Occupation.......... Working.......... Not Working.......... Weekly Wage..........
Dependents.......... Children.......... Rent..........
Family History..........
....
Past History..........
....
Present History..........
....
Principal Symptoms..........
Menstruation..........
Discharge.......... Pain..........
Frequency of Urination..........
Genital Sores.......... When.......... Duration..........
Secondary Lesions.......... How Long Treated..........
Kind of Treatment.......... Reflexes..........
External Genitals..........
Glands.......... Skin..........
Skene's Glands—1.......... Urethra—2..........
Bartholin's Glands—3.......... Vagina—4..........
Cervix—5.......... Cervical Canal—6..........
Uterus.......... Tubes.......... Ovaries..........
Cystoscopy..........

SMEARS

DATE	Result	DATE	Result	DATE	Result

URINE

DATE	Sp. Gr.	React.	Alb.	Sug.	Functional Test	Microscopical

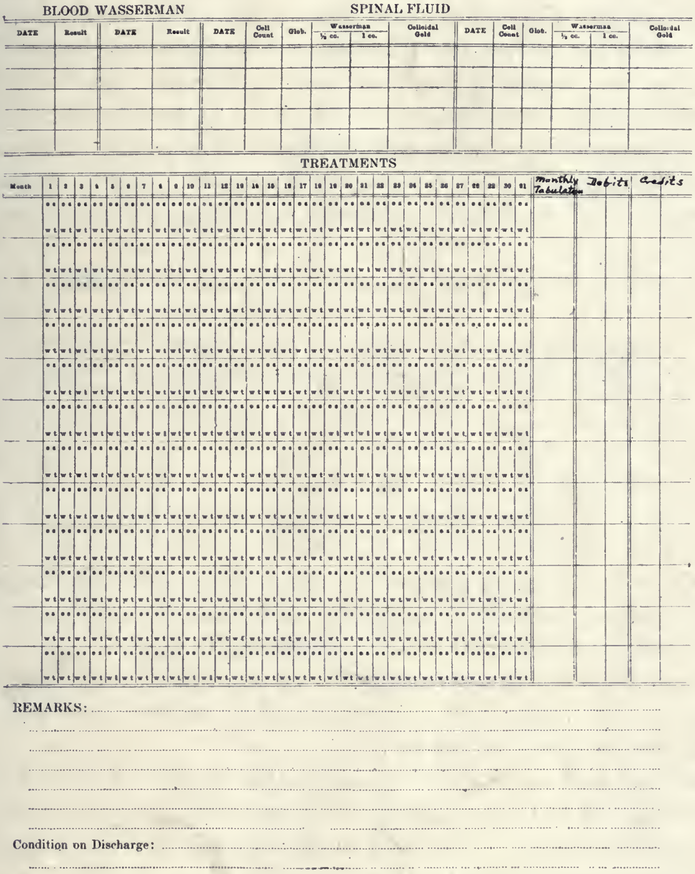
DIAGNOSIS
....
....
....
....

Fig. 7.—Original blue.

The only duplication in the present system is in the social history and this will likely be eliminated soon.

The Clinical Record Card, which is the chief source of information concerning the patient, combines simplicity with detail and efficiency. It is largely the result of many years' experience and experimenting in the office of the Director. The cards are 8½ x 11 inches, blue for female and white for male patients.

The obverse of the card is used for the history of the case. This includes the patient's name, address, aliases, serial numbers, etc. A brief social history follows the above information and will probably soon be eliminated. Besides sufficient space for family history, past history and the present illness the card is blocked off for a detailed examination.



BLOOD WASSERMAN

SPINAL FLUID

BLOOD WASSERMAN				SPINAL FLUID											
DATE	Result	DATE	Result	DATE	Cell Count	Glob.	Wasserman ½ cc.	Wasserman 1 cc.	Colloidal Gold	DATE	Cell Count	Glob.	Wasserman ½ cc.	Wasserman 1 cc.	Colloidal Gold

TREATMENTS

Month	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	Monthly Tabulation	Debits	Credits
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REMARKS: ....

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Condition on Discharge: ....

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Fig. 8.

The male and female cards differ in this respect only as the parts examined differ, but the female cards have a space devoted to the many smears required from time to time.

It is the reverse side of the cards which merits special attention.

The upper part of the card is arranged for recording the blood and spinal fluid findings. Below this and occupying about three-fourths of the card are transverse rulings for the months of the year and vertical rulings for the days of the month. The grilling effect thus produced leaves small rectangular spaces opposite the months and below the days in the angles of which are printed the small letters e = examination, w = Wassermann, t = treatment and s = smear. The physician as he sees the case, merely checks one or more of the letters to indicate just what he has done and with pen and ink writes in the blank center of the rectangles the kind of treatment given. The following enlargement of the small rectangles will serve to illustrate the method of use.

The interpretation would be: on June 1st the patient was examined, had a Wassermann and received treatment. The treatment consisted of a protargol irrigation and he was supplied with a syringe and protargol solution for home use.

Month	1	2	3
June 1922	[✓ e] s Pro Syr [✓ t] [✓ w]		

When the cards are returned to the statistical clerk she refers at once to this space, makes a record of what was done and posts the charge against the patient.

With this system of daily recording the operation of this Clinic we are enabled to make a detailed report at the end of each month, and have this report in the mail to the State Department of Health on the first day of each month.

TREATMENT

Gonorrhea in the Female.—Gonorrhea in women receives very thorough and painstaking treatment in this Clinic. The method is about as follows: The patient is prepared on the table in the lithotomy position by the nurse attending. The external genitals are cleansed. The urethra is irrigated with silver nitrate solution by means of an asepto syringe. The lips of the urinary meatus are separated either with the fingers of the left hand or by means of a self-retaining retractor. The ducts of the periurethral glands, and of Skene's glands, are sought out, a blunt needle is inserted and the glands irrigated with protargol solution using a two c.c. Luer syringe. The ducts of Bartholin's glands are next found and treatment followed as above. The speculum is then inserted and the vaginal walls wiped with cotton swabs on applicators. The cervix and cervical canal are treated with iodine swabs. This treatment is carried out every day except Wednesday and Sunday. Douches of weak protargol solution are prescribed in the interim.

The test for cure is the absence of pus from the meatus after stripping, from the cervical canal and from the gland structures. Smears from these sites must also be gonococci negative on three consecutive occasions.

Gonorrhea in the Male.—The acute, uncomplicated case is treated in the following manner: The patient is supplied with an asepto syringe and a bottle of protargol solution for home use and instructed to use it about every two hours. The daily irrigations are begun at once, a mild protargol solution being preferred until the gonococci disappear. A mild potassium permanganate irrigation supplants the protargol and in the terminal stages silver nitrate is used, as are sounds and massage.

Complications and chronic cases are treated according to their indications. Epididymitis cases are all interned in the hospital and confined to bed. Bridge support and moist heat are usually successful, but if not, operation is resorted to.

The test for cure is the absence of discharge from the urethra, a clear first and second urine, negative prostatic and seminal secretion and a canal free from infiltrations and other pathology.

Chancroid.—All ulcers and suspicious lesions are subject to repeated dark-field examinations. Chancroidal ulcers are thoroughly cauterized with pure phenol and dusted with iodoform powder. Buboes, when fluctuating, are opened and drained.

Treatment of Syphilis.—When the diagnosis of syphilis has been made, the patient is so advised and the treatment outlined for his direction. This consists of six weekly intravenous injections of arsphenamine or neoarsphenamine, and twenty bi-weekly intramuscular injections of the succinamide of mercury gr. 1/6.

The intravenous treatments are administered on Wednesday mornings. At this time the entire staff unites in the Male Clinic and devotes the whole morning to that work. Men and women are treated in the same clinic and on the same day, but effort is made to treat them at different times. Mixing of patients is here necessary because of a lack of proper room.

The mercury injections are given on Mondays and Fridays. These treatments are administered in the respective clinics by the physician on duty there.

When the course of six intravenous and twenty intramuscular injections have been given the patient is advised to rest for three weeks, after which time he returns for blood test. If the Wassermann is reported positive the course is repeated entirely, if negative the entire course may be repeated according to the indications, or the mercury course alone be given. All subsequent treatments are guided largely by the blood and spinal fluid findings. The case is closed as arrested when the blood has been negative for two years and the spinal fluid is negative. Check Wassermanns are done at periods of every three months on arrested cases in the first year and at six month periods in the latter years.

Neural syphilis is at present being treated with the hypertonic salt solution followed six hours later by neoarsphenamine. A modified Swift-Ellis treatment was used previously and will be resumed if the present method proves valueless.

Wassermann-fast cases are now being treated with silver arsphenamine but our results are, as yet, uncertain.

Nonvenereal Cases.—Unfortunately our operating facilities do not allow us to perform major operations in the clinic. Most of these cases are referred to other hospitals. However, most of the minor things are done here. Intravesical operations through the cystoscope are performed and all, where it is indicated, are subject to cystoscopic and endoscopic examination. If, as we hope is the case, a new hospital is possible in the near future, we will not be forced to lose sight of any case that may come to us.

SOCIAL SERVICE

There are a great many demands upon the time of the social worker. The financial status of applicants must often be verified, because there are always those who are seeking something for nothing. Social conditions must frequently be studied at first hand and addresses have to be confirmed and corrected. Whenever possible the source of infection is traced.

The follow-up work devolves upon the Social Service Department. Once a patient registers in the clinic, he is thereafter under our control, unless properly discharged by the attending physician. If, as very often happens, the patient grows lax in his attendance and has been delinquent for some time the statistical clerk attaches a metal signal to his card. The social worker then mails the patient a notice requesting him to return to the clinic. If he fails to respond to the first notice, a second signal is fixed to the card and a second letter sent, this time threatening police intervention. These two notices account for about 70 per cent of the delinquents, the other 30 per cent being influenced by a direct call from the social worker or by the police.

When prostitutes have been released from either the hospital or the Detention Home they are required to return once a week thereafter, on a day assigned to them, for examination. In the event of their failure to report regularly the social worker notifies the "Vice Squad" and the delinquent ones are brought in.

In all its activities the Social Service Department is greatly assisted by the "Vice Squad" of the regular police and the Sanitary Police of the Division of Health. These two organizations lend invaluable authority to the work in this department.

DOES IT PAY?

In the operation of a business or an institution, the test of its value lies in the dividends it pays. Taking an institution, such as the Venereal Control Clinic, it is difficult to find a suitable standard of comparison to compute its worth to the community. Monetary standards are the usual basis for the determination of the success of any enterprise. It would seem hardly fair to apply that sort of a test in an institution such as ours, but even in that material sense the clinic is not a failure. There are yearly quite considerable sums turned into the City Treasury, moneys collected in small fees from those who can pay a little for their services. Our dividends, however, are not paid in dollars and cents.

The accompanying table shows the developmental growth of the clinic from its inception through the year just ended.

DATA	JULY 7, '18 TO AUG. 15, '19	JAN. 1, '20 TO DEC. 31, '20	JAN. 1, '21 TO DEC. 31, '21
Number of treatments administered to ambulatory and interned patients.	7653	14,923	27,110
Number of patients interned.	201	829	949

While there has been a constant increase in the number of patients admitted, due to the publicity the Clinic has had, there has been a more marked rise in the daily attendance. The total daily calls for the six-month period ending June 30, 1922, amounts to 21,388, an average of about 120 daily. This has been due largely to the industrial depression through which we have been passing. Rendering service to these unfortunates, who could not possibly have had attention in private offices, is one of our big duties and truly a humanitarian one.

It is difficult to see the actual good such an institution as this does for the community which it serves, for the picture is more or less confusing to the casual observer. To him the rapid gain in attendance would seem to mean that the venereal diseases are on the increase, whereas it is in reality a testimonial to the usefulness of the Clinic. But aside from the fact that the scope of the Clinic's service is expanding in its influence, there is one bit of tangible evidence embodied in the Annual Report of last year, which shows that we have, in part at least, accomplished the purpose of the institution. It says, ''We have taken care of 621 police cases—and only 31 per cent of them were infected—while in 1919, out of 52 girls taken in one raid *only one* was *not* infected.''

Inasmuch as the prostitute has been considered the great fountain-head from which most of our venereal diseases are spread: where future husbands, as well as present ones, for the most part contract the malady which they will later transmit, quite unwittingly sometimes, to innocent and virtuous wives, it would seem that we have, in a way at least, diminished the risks these wives must take. It is an absolute and incontrovertible fact that known prostitutes in Toledo are, at present, the least source of danger under current management. The greatest source of danger lies in the unknown, who do not come under the observation of the police.

It has only been through the cooperation of our City Administration, Department of Health and Police Department, and also by the aid of the State Board of Health that we have been able to establish and maintain the quarantine system of prostitutes, and otherwise make this Clinic a success.

The Staff:

D. W. Iford, M.D., Commissioner of Health.
John G. Keller, M.D., F.A.C.S, Director.
L. A. Willoughby, M.D., Assistant Director.
E. W. Huffer, B.S., M.D., Assistant.
L. L. Rosenberg, B.S., M.D., Assistant.
Catherine M. Mapes, R.N., Chief Nurse and Superintendent.
Blanch C. Ward, R.N., Social Service Department.
Mary Mallett, Stenographer, Bookkeeper and Statistical Clerk.
Seven Graduate Nurses.
Two Male Nurses.

SYPHILIS OF THE ADRENALS

By Wm. H. Deaderick, M.D., F.A.C.P., Hot Springs National Park, Ark.

(Received for publication, July 1, 1922)

LUETIC lesions of the adrenals in congenital syphilis are not rare and such lesions are frequently found in recent years at postmortem in cases of acquired syphilis.

The marked asthenia sometimes observed in the course of syphilis has been attributed to luetic invasion of these glands.

The dangers of arsenical treatment of syphilitic suprarenal disease have been recognized and it is possible that the benefits derived from adrenalin in combating certain of the reactions of arsphenamine, indicate the presence of such lesions though unsuspected.

Syphilis of the adrenals was recognized pathologically, especially in hereditary syphilis, before any clinical cases were reported.

Lancereaux[1] states that "the suprarenal capsules are remarkable in a great number of the cases of hereditary syphilis for a very evident increase in size. Virchow has ascertained this increase in size in children affected with congenital syphilis and observed, moreover, in one case complete fatty degeneration of these glands. Baerensprung found under the same circumstances the cortical substance of the suprarenal capsules invaded by masses of nuclei and young cells of conjunctive tissue, a modification very analogous to the diffused lesion of the liver. Hyperemic from the first the suprarenal capsules have never presented, later, the white miliary points so frequent in the liver."

Discussing hemorrhage into the adrenals having undergone fatty degeneration, Merkel[2] says, "Here we are almost led to conclude that we have to do with congenital syphilis in connection with which Virchow has found similar conditions. In addition to this form of fatty degeneration which Von Baerensprung (1864) and Huber (1869) confirm, gummata are described in congenital syphilis by Virchow and Hecker (1869). We do not possess any further definite information as to how syphilis subsequently attacking the suprarenal capsules is indicated clinically or how it is anatomically manifested. According to Baerensprung and Huber, the suprarenal capsules are found on inspection to be considerably swollen, hyperemic and beset with granules or spots, small, white, miliary, and the size of a poppy seed, which traverse the cortical substance in the form of radiating striae. These spots and granules are found to be masses composed of nuclei and young cells. In another case (a syphilitic child nine days old affected with sclerosis) Hecker records a peculiar cartilaginous consistence of the suprarenal capsules and a uniform gray infiltration of the parenchyma.''

Ribadeau-Dumas and Pater[3] studied the suprarenal capsules in twenty cases of hereditary syphilis, and although in some cases the research was fruitless, they were relatively frequently affected and very often a peculiar affinity of the treponema for this gland could be demonstrated. The lesions met with were of the following types: simple hyperemia, congestion with infective nodules, sclerosis, atrophic and sometimes cellular changes, simple necrosis, gumma and sclero-gummatous degeneration. The treponema was very frequently found in the suprarenals. They conclude that suprarenalitis is one of the elements in the pathologic picture of congenital visceral syphilis.

Marshall and Ffrench[4] declare that ''evidence of inherited syphilis has been found in cases of infantilism, dwarfism, gigantism, myxedema, acromegaly, exophthalmic goiter and Addison's disease, and cases have been reported in which treatment by mercury or salvarsan caused improvement in these conditions.''

In acquired syphilis Lancereaux[5] says that ''like the thyroid body the suprarenal capsules are, in general, enlarged in persons who succumb to the attacks of visceral syphilis; such at least results from the observation of Professor Virchow as well as from our own. In addition to the increase in size the learned Professor has observed in one case a complete fatty degeneration of these glands, which were also found occupied by tumors which might well be nothing other than gummy deposits.''

Sir Dyce Duckworth[6] stated that amyloid or lardaceous degeneration of the adrenal bodies may occur in syphilis.

Rolleston[7] affirms that ''single or, more rarely, multiple small gummata are occasionally seen in the suprarenal bodies, and general fibrosis may be due to the syphilitic poison.''

Neusser[8] says that ''chronic productive inflammation characterized by new formation of connective tissue and partial atrophy of the parenchyma has been observed as a manifestation of syphilis. * * * Syphilis occurs occasionally in the form of a typical gumma composed of granulating tissue terminating in central necrosis and peripheral cicatrization. As mentioned above it may be manifested atypically in the form of a cirrhotic inflammation. Sometimes it is with difficulty differentiated from tuberculosis. Syphilitic thickening of the vessels is also observed.''

McIntosh and Fildes[9] announce that ''the suprarenal glands are one of the sites of predilection of the Spirochaeta pallida. In a considerable number of these glands there are well-marked histological changes. The striking feature is a small-celled infiltration of the medulla, which in some cases is so severe that small necrotic areas are produced. There is usually a slight hyperplasia of the connective tissue, but sometimes this is so well-marked as to cause fibrosis of the whole organ. In a certain number of the cases, the glands, apart from a slight venous congestion, may be said to be normal. * * * In the suprarenal gland the spirochetes seem to be distributed fairly evenly through the medulla and cortex, though there is always the marked preference for epithelial cells and perivascular structures.''

Osler and Gibson[10] assert that ''amyloid changes are not infrequent when the change exists in other organs. Gummata have been described and interstitial changes.''

In a remarkable article by Warthin[11] on the pathology of syphilis, he described the adrenal lesions as follows: ''Small infiltrations of plasma cells and lymphocytes are of constant occurrence in the adrenals of cases having known syphilis and unsuspected latent syphilis. In the great majority of cases these infiltrations are slight. They occur usually in the medullary portion or in the inner portion of the reticular zone of the cortex. They are usually perivascular. Fibroblastic proliferation of the stroma or fibrosis may or may not be present; the capsule of the organ is usually thickened, and perivascular infiltrations of small size occur in the surrounding tissues. The walls of the blood vessels usually are thickened. Very rarely the infiltrations are so marked as to assume the characters of miliary gummata. Caseating gummata with giant cells have not been seen. In three cases the syphilitic infiltrations and fibrosis were so marked as to have caused nearly complete atrophy of the greater part of the organ. All three of these cases presented the symptom complex of Addison's disease. In one of these cases marked syphilitic infiltrations occurred also in the adrenal and semilunar ganglia. With the exception of these three cases no symptoms were observed that could be directly ascribed to the syphilitic changes in the adrenals. Whether in the less severe cases disturbances of adrenal function may be responsible for the low blood pressure seen in some of the cases, it is, of course, impossible to say. Another striking feature of the adrenals in chronic syphilis is the marked lipoidosis of the cortex seen in so many cases. This lipoidosis may be patchy, involving certain circumscribed areas in the cortex, or it may involve the entire cortex. The cells are filled with numerous, large, doubly refracting droplets that stain a brownish red with Sudan 111 and Scharlach R; with osmic acid many of the droplets take no stain, while others are grayish brown. The significance of this lipoidosis is not apparent, nor is its relation to syphilis. It is probably to be interpreted as an expression of a cholesterolemia or cholesterol retention, as a feature of a general disturbance of metabolism.''

Lespinasse[12] says that ''amyloid degeneration of the suprarenal glands is not uncommon. Interstitial changes take place and localized or diffuse gummatous inflammations are observed. The cellular infiltration so characteristic of syphilitic processes, is slight, in the majority of cases. The medulla of the inner portion of the reticular zone of the cortex is generally affected. The capsule is usually thickened and infiltration and fibrosis may be so intensive as to cause marked atrophy of the gland, simulating Addison's disease. Gummata are frequently present and are usually miliary in type. Treponemata pallida are abundantly present in congenital syphilis involving the parenchyma.''

On the clinical side Eichhorst[13] states his belief that ''at other times tuberculosis or carcinoma in other organs, antecedent syphilis, suppuration or other wasting discharge may suggest that the adrenal bodies are the seat of tuberculosis, carcinoma, gumma or amyloid disease with consequent development of Addison's disease.''

Neusser[8] declares that "in a certain sense the possibility of treatment based on etiology is afforded by syphilis but unfortunately cases of Addison's disease thus caused are of rare occurrence."

Writing on Addison's disease Dock[14] says that "tuberculosis and syphilis have their specific causes."

Barker[15] states that "in other cases (of Addison's disease) syphilis or atrophy of these glands has been observed."

And in another place[16] "in most of the cases of Addison's disease upon which postmortem examinations have been made tuberculosis of the suprarenals has been found; in others, neoplasm, syphilis, or atrophy was responsible."

Riesman[17] avers that "Addison's disease is usually due to tuberculosis of the adrenal glands; in rare instances to syphilis, fibrosis or tumor."

Turning to the reports of clinical cases, Gordon[18] details probably the first case in an adult which he saw with Wales. The patient was a young man who, following a genital lesion, developed anemia, sore throat, fissures of the tongue, coryza and fissures and condylomata around the anus. A diagnosis of syphilis was made. Later the skin became dirty yellow with dark spots on the scrotum and frequent nocturia. A month later diarrhea began and a soft systolic bruit was heard, the vision was impaired, vomiting of bilious matter ensued and palpitation of the heart was troublesome. He died a few weeks later. At postmortem examination the suprarenal capsules were found about equal in size, three and one-half by one and one-half inches and weighed 70 grains. They were friable and nodular and contained a cavity with semifluid contents of a dark brown color. A pathologist expressed his belief that it was syphilis.

Schulmann[19] credits Gaucher with having reported the first case in 1880, the details of this case, however, are not accessible to me.

Rolleston[20] records Beavan Rake in 1889 as having described Addison's disease in a syphilitic Hindoo who was also the subject of leprosy but gives no further details.

The patient of Jaquet and Sezary[21] was a man aged 66 who died in the midst of the secondary period. Four months before he had been treated for a chancre with a papular syphilide of the scrotum but he soon presented a generalized eruption. At the same time a serious asthenia kept him in bed accompanied with violent pains in the lumbar region and lower limbs, anorexia and cutaneous pigmentation. Specific treatment caused some improvement but a short time later he returned with a recurrence of the scrotal syphilides and pains in the lower limbs. Some days later he died of cerebral hemorrhage. The internal organs were examined very minutely. Lesions appeared only in the lungs and suprarenals, the latter being very interesting. They were enormous, hard and apparently without trace of postmortem change. Sclerosis radiating from the fibrous shell toward the medulla was manifest and lymphocytic infiltration was abundant. The pigment was very much increased. On examination by the Levaditi method the treponemata were seen to abound, especially in the fascicular zone and were located both inside and between the cells, forming masses in the connective tissue. A few were found in the blood vessels. They were not all spiral, some being stretched out and granular. There were none in the medullary substance, nor could treponemata be found in the scrotal lesions or the inguinal glands. The syphilitic infection of the suprarenals had perhaps been prepared and facilitated by a slight tubercular lesion which existed in the right lung.

Schaffner and Howard[22] report a case in a man of 38 who was troubled two years previously with a loose cough and an attack of vomiting. Later he suffered from a sensation of numbness in his hands and feet and shortly noted that his skin was becoming dark, particularly on the forehead, neck and axillae and in the anticubital inguinal and popliteal fossae and the waist line. The lungs showed signs suggesting tubercular infection of both apices. The blood pressure was 98 systolic and 80 diastolic. The sputum contained no tubercle bacilli. The Wassermann was a double plus. The patient was immediately placed upon antisyphilitic treatment consisting of salvarsan and mercury. He responded immediately to the specific treatment, improved steadily, gained 19 pounds in weight, with corresponding changes in his color.

Blum[23] reports the case of a woman, aged 25, infected with syphilis one month previous and had received eleven injections of biniodid of mercury which was followed by stomatitis and a polymorphous eruption; for ten days her temperature varied from 39° to 40°. An abrupt fall in temperature was then followed by a pseudoperitoneal syndrome, hypotension, asthenia, hypothermia, vomiting and the white line. Treatment for eight days with adrenalin caused the disappearance of the symptoms.

The case of Castex[24] was in a woman of 42 who had been operated upon at 21 for an abdominal cyst when both ovaries were removed. The present illness was preceded by icterus lasting several months followed by pain in the hypochondrium and vomiting. Within a year the abdomen had become prominent and the anus and legs smaller; she suffered from headaches and tired easily. She now presented considerable deformity of the trunk; the skeleton was sensitive to pressure, especially in the extremities, also in the thorax and pelvis. The vertebral column showed kypho-scoliosis with preternatural mobility. The skin was discolored, the linea alba was markedly pigmented and leucoderma existed. Strabismus, irregular pupils, multiple corneal opacities and defective hearing were noted. The thyroid and lymphatic glands were not palpable. Asthenia was very marked and the deformity of the trunk seemed to be progressive. In spite of the negative Wassermann reaction other syphilitic stigmata were present; cutaneous scars, dorsal leucoderma and loss of hair at the temples and of the eye-lashes. There was a slight systolic murmur accompanying the first heart sound and the aortic second was metallic. The cardiac and aortic dullness was somewhat increased. The patient presented the symptoms of chronic capsular deficiency, that is, asthenia, adynamia, general cutaneous pigmentation and gastric disturbances of the suprarenal type. Mercury and iodin caused some improvement.

Thompson[25] saw one case with a typical Addison syndrome and a four-plus Wassermann reaction that died in spite of vigorous antisyphilitic treatment.

Huebschmann[26] has reported two cases. In one, notwithstanding pathologic findings in the adrenals which rendered a diagnosis of syphilis probable, the Wassermann reaction was negative. As a result of this experience and that of Fahr and Reiche who reported the Wassermann negative in the presence of undoubted syphilitic adrenal lesions, Huebschmann raises the question as to whether or not disease of these organs may so influence the sera of syphilitics as to render them Wassermann negative. He believes this possible on account of the relationship of the Wassermann reaction and lipoids on one hand and of lipoids and the adrenal system on the other.

The following case is reported as one of probable Addison's disease of syphilitic origin.

The patient was a white female, aged 40, a decided brunette, and of good nutrition. Her family history was unimportant. She had diphtheria 12 years ago and her appendix and a cyst of the right ovary were removed 11 years ago. She married her first husband 18 years ago and lived with him six years. She thinks he was free from venereal disease. She married her present husband eight years ago. He is now 52 and admits luetic infection 28 years ago with insufficient treatment. She has had three miscarriages but no full term labors. Nine years ago she had pains in the liver region followed by marked jaundice which was very persistent. She does not know exactly when the jaundice disappeared or when the present pigmentation began. She realizes the marked difference in the appearance of her skin then and now and believes the present pigmentation the outcome of the jaundice but is not clear as to the time of transition. For the past seven or eight months she has had vomiting attacks preceded by nausea. At first these attacks came on from one to three times a week, then became more frequent until they occurred after almost every meal. She has lost 15 lbs. during this period. For eight months she has been very weak and at times feels "as helpless as a baby." During some of the "weak spells" she is able to sit up, but frequently is compelled to lie down, being too weak to sit. She has had dyspnea on exertion for several years. Seven months ago she consulted two throat specialists on account of sore throat and enlargement of the cervical glands. Both diagnosed syphilis and one prescribed antiluetic treatment by mouth which she took for two and a half months causing resolution of the throat and gland trouble. About two months ago she noticed a cloudiness of the right cornea.

Her present complaint is pigmentation of the skin, pain in the right hypochondrium and precordia, backache, weakness, vomiting, and constipation. The menses are normal. The examination showed cutaneous pigmentation disseminated over most of the body. The intensity of the color for the most part varied directly with the size of the patches, being darkest over the large patches and lightest over the smaller and ranged from light brown in the latter to chocolate in the former. Anteriorly the darkest patches were in the axillae, elbows, crotch, around the waist line and on the thighs and legs. The normal areolar pigmentation of the breasts was absent and over and immediately around each nipple was a patch of very dark pigment. Distributed over the chest and neck were light colored patches varying in size from large freckles to that of a small coin. Posteriorly the distribution was particularly thick over the scapular regions, arms, thighs and legs. The lateral aspects of the arms, hips and legs were deeply pigmented.

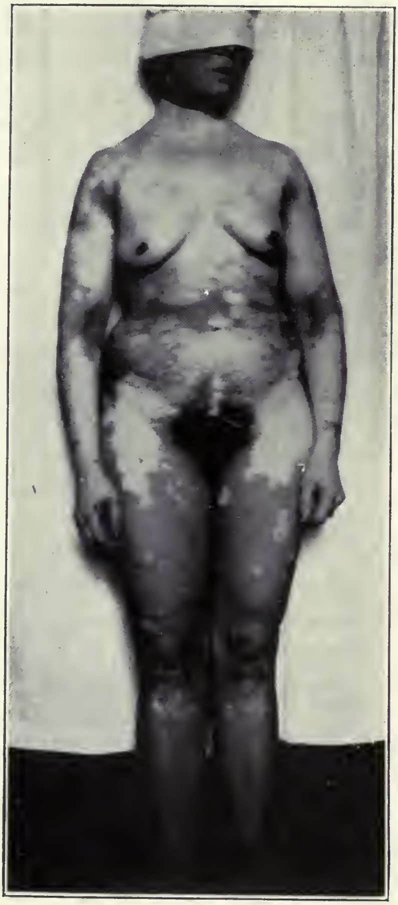

Fig. 1.

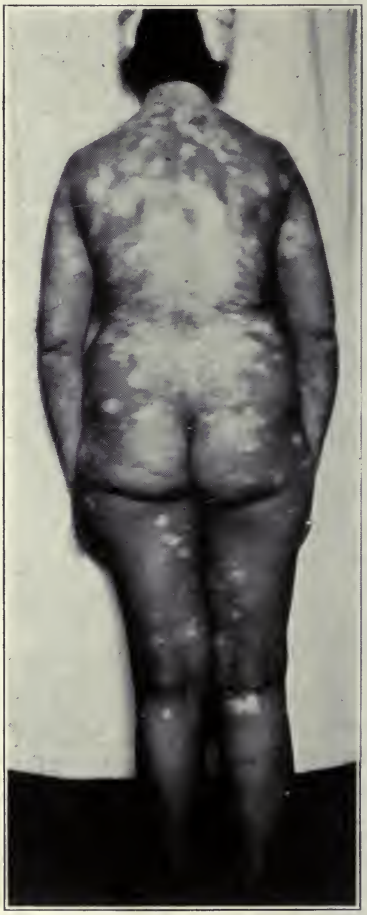

Fig. 2.

On the face the dark discoloration was particularly under the eyes, over the bridge of the nose and on the cheeks. The hands showed small areas at the bases of and between the fingers. Between the pigmented areas the skin appeared whiter than normal and in places leukodermatous. There was no pigmentation of the buccal mucous membrane but this was present on the vulva, including the inner aspects of the labia minora, shading off into the bluish discolored vagina. Sergent's white line was not evident.

The pulse was 94-108, otherwise normal. The blood pressure was 100 systolic and 65 diastolic. Ten minims of a 1:1000 solution adrenalin chlorid caused an elevation of the systolic pressure to 110 in 15 minutes. The temperature ranged from 99.4° to 100.2°. The lungs were normal throughout. The apex beat of the heart was normally situated; there were no adventitious sounds and the area of dullness was not increased. There was slight tenderness in the gall bladder region and considerably more in the right lumbar. The area of liver dullness was not increased. The lower and upper tendon reflexes were not disturbed and the pupils and Romberg were negative. Corneal ulceration was present in the lower nasal quadrant over the right pupil. The uterus was anteflexed, freely movable, the fundus enlarged but not tender. There was no lymphatic enlargement. In the mouth were several dead and crowned teeth. The Wassermann reaction was two-plus, the urine negative except for bile, the blood sugar .110 per cent, the alkali reserve 8.0 and the alveolar air tension 35. The hemoglobin was 76 per cent (Dare), the erythrocytes 3,850,000, the leucocytes 5,680 and the differential count: polymorphonuclears 61 per cent, lymphocytes 31 per cent, large mononuclears 6 per cent and eosinophiles 2 per cent.

The treatment consisted of daily intramuscular injections of the benzoate of mercury up to one-third grain and of the oral administration of suprarenal gland. On discharge after three weeks' treatment all the systemic symptoms were improved but no change could be detected in the cutaneous pigmentation. A month after discharge she reported that the discoloration was fading.

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PRACTICAL OBSERVATIONS ON SYPHILIS. V

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Section 16

Syphilis of the Eye—Acquired Form

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EYELIDS

SYPHILIS in any stage, from the primary sore to late gumma may be met with in the eyelids.

THE TARSUS

The tarsus is liable to syphilitic infection in the late stages, either in the form of circumscribed nodes, or a diffuse gummous infiltration, in which condition the lids become so thick that it is impossible to evert them. This condition shows little tendency to break down.

CONJUNCTIVA

Primary lesions occur rarely, the relatively most frequent seat being the conjunctiva of the lower lid and transition fold. The lesions present a lardaceous swelling of the conjunctiva, with slight irritation and edema associated with profuse mucopurulent secretion.

A few cases have been reported of chancre of the bulbar conjunctiva, in which the lesions closely resembled, at first, a phlyctena. In the late stages papules, either single or multiple, have been described. They show small tendency to break down, and disappear under antisyphilitic treatment. As a rule gummata create more or less irritation as they involve the underlying structures. De Schweinitz calls attention to a particular type of conjunctival inflammation occurring in subjects of pronounced syphilis (conjunctivitis syphilitica) in form of granulations similar to trachoma follicles. This condition does not respond to local treatment, but does to antisyphilitic treatment.

SCLERA

Gummata of the sclera, *per se,* are of such rarity that most of the text books devote little attention to a description of them.

The gumma may spread to the ciliary body, producing a cyclitis and if situated near the cornea it may also become involved. If untreated, the gumma may ulcerate, causing perforation and loss of the eye.

NASAL DUCT

Stricture of the nasal duct may occur as a consequence of luetic periostitis of the lacrimal canal, or extension from the nasal cavity.

CORNEA

Acquired syphilis seldom attacks the cornea; however, certain pathologic changes do occur, whose etiologic factor can be traced to the acquired form. Keratitis punctata syphilitica, described by de Schweinitz, Mauthner, Fuchs and Heck, appears in the later stages of the disease, and is characterized by the presence of minute circumscribed grayish white spots in the parenchyma of the cornea, usually confined to the center. These spots generally disappear without leaving any trace. The condition is unaccompanied as a rule by iritis or any circumcorneal injection.

DEEP VASCULAR KERATITIS

Deep vascular keratitis, though occurring in both forms of lues, is probably met with more frequently in the acquired form. It appears as a pale red patch occupying a small portion of the circumference of the cornea, rarely over one quarter and seldom covering the pupillary area. Examination under the corneal loupe discloses minute blood vessels, beginning at the corneal margin and extending into the deep layers of the substantia propria, which is more or less cloudy for a distance around the vessels. It is accompanied by symptoms of irritation, photophobia and disturbance of vision. The condition is of a more or less chronic duration, the cornea finally becoming transparent again. (Weeks.)

NEUROPARALYTIC KERATITIS

Neuroparalytic keratitis is generally conceded to be due to atrophic disturbance of the trigeminus, consequently this condition can be at times traced to syphilitic deposits, along the course of the nerve. In this form of keratitis, a grayish infiltration of the cornea first takes place in the center which generally spreads until the entire cornea may become involved with the exception of a narrow margin around the limbus, which usually remains free. Sloughing generally follows with the loss of the entire cornea. A striking fact is that the eye shows practically no irritation, ciliary injection is present, there is no lacrimation and the patient does not complain of pain. When tested the cornea is found to be insensitive.

Gumma of the cornea has been reported, but is exceedingly rare.

LENS

Following any inflammation of the ciliary body, the nutrition of the lens is liable to be interfered with, in which case it is apt to become opaque. For this reason, individuals affected with syphilis are more prone to cataract than those unaffected with the disease.

UVEAL TRACT

Bearing in mind the anatomic, physiologic and pathologic continuity of the different portions of the uveal tract, it seems scarcely conceivable that an inflammatory condition can be strictly limited to a single part; nor is this so.

IRIS

As early as five or six weeks after the initial lesion, the roseola syphilitica has been observed in the iris, and in some cases even before the appearance of the cutaneous eruption (Roemer). Clinically localized hyperemias are seen in the center of the iris, which portion is abundantly supplied with minute vessels, and are supposed to be due to capillary emboli of treponemata. How often this condition occurs is difficult to ascertain, owing to the fact that it causes no trouble in the iris and quickly disappears.

Syphilis has been found to be the etiologic factor in from 40 to 70 per cent of all cases.

Iritis in all its forms, from whatever cause, presents certain conditions in common; viz.; pericorneal injection, due to injection of the anterior ciliary vessels producing the characteristic deep pink color. In conjunction with this the conjunctival vessels are always engorged, turbidity of the aqueous due to exudate, blood or pus. Change of color in the iris is pronounced, due to the congestion and swelling whereby the iris pattern is obliterated, producing the well-known "muddy iris." The pupil is contracted, due, in part, to hyperemia and in part to irritation of the peripheral nerve filaments. Formation of posterior synechia or attachments between the anterior capsule of the lens, and the iris vary in size, number and firmness. The iris may be bound down throughout the entire pupillary margin by the inflammatory process. These inflammatory bands are easily demonstrable by the instillation of atropine, giving the characteristic irregular pupil of iritis. The pain is severe, throbbing in character, not confined to the eye itself, but extending to the temple and down the side of the nose and at times extends even to the teeth. The vision is disturbed in proportion to the amount of cloudiness which occurs in media.

IRITIS PAPULOSA OR TRUE SYPHILITIC IRITIS

In the form of syphilitic iritis described in the preceding paragraphs etiologic diagnosis could be made only after a thorough physical and biological examination of the patient. This is not the case in iritis papulosa; here the eye presents certain well-defined clinical signs which immediately suggest lues to the examiner.

There is a high degree of injection of both conjunctival and ciliary vessels. The iris is discolored and its pattern obscured to a moderate degree. Examination with oblique illumination reveals the pressure of the nodules situated usually at the pupillary border of the iris, although they are occasionally seen near the ciliary border or even in the tissue between. They present a yellowish red or brown color and are about the size of the head of a pin. These nodules project into the anterior chamber or pupillary space. Focal illumination also brings out posterior synechia.

Microscopic studies bring out the fact that there is no sharp line of demarcation between specific and plastic iritis and iritis papulosa, as it has been demonstrated microscopically that there are nodules present in all cases of plastic iritis which clinically give no sign, being too minute to be observed.

GUMMA

This condition occurs in the late stages of the disease and is of greater rarity than the papule. It is usually a solitary tumor of considerable size and appears almost always at the ciliary margin of the iris; is usually seen in only one eye. The iris is more or less involved as is the ciliary body. It may undergo degeneration or may proliferate and fill the anterior chamber or it may perforate the sclera by extension through the ciliary body.

Examination of the cornea in the vicinity of the tumor will generally show a slight haziness and the formation deposits in Descemet's membrane. In case of recovery a scar is left in the shape of atrophy of the iris fibers at the site of the tumor.

CILIARY BODY

Inflammations restricted to the ciliary body alone are exceedingly uncommon, owing to the intimate relationship between this structure and the rest of the uveal tract. Syphilitic cyclitis is essentially an iridocyclitis of the plastic type. The disease is acute, both eyes being affected, though not always simultaneously.

The symptoms leading to a diagnosis are the following: circumcorneal injection, neuralgic pains radiating from the eye through the head, extreme tenderness upon pressure over ciliary region; turbidity of the aqueous, posterior synechia binding the iris to the anterior capsule of the lens; a deepening of the anterior chamber; exudate or blood in the anterior chamber; opacities in the anterior layers of the vitreous, and deposits of exudation on the posterior layer of the cornea.

CHOROID

Next to iritis, choroiditis is the most common luetic manifestation in the eye. The disease assumes the exudative form, and, whereas it is generally disseminated in character, yet it may be diffuse, circumscribed or central, hence it is not safe to attempt to make a diagnosis of syphilis by the appearance of any one particular form of choroiditis.

It occurs usually in the early stages of the disease, anywhere from the fourth month to the second year, although it may not appear until later. Both eyes are usually affected, and the disease runs a chronic course, lasting over a period of six weeks to three months or more. If seen in the early stages, the ophthalmoscope reveals the recent foci of inflammation as well-defined yellowish or grayish spots scattered throughout the fundus; occasionally retinal vessels can be seen to pass over them. These spots are due to infiltration of the choroid. The overlying retina is slightly cloudy and edematous. Small diffuse opacities are seen in the vitreous, usually in the posterior portion, owing to the exudate having passed through the retina. In the later stages the exudate in choroid becomes organized, forming fibrous tissue which more or less destroys the normal structure of the choroid and overlying retina, so that the color of the spots gradually changes to white, due to atrophy of the choroid and retina, whereby the sclera is seen to shine through. In the last stages, masses of pigment are seen shaped around the edges of the atrophic areas. The symptom which first attracts the patient's attention is the diminution of vision.

The prognosis should be guarded owing to the fact that there may be an extension of the disease to the retina and optic nerve, or forward to the ciliary body and choroid.

RETINA

Syphilis may manifest itself in any one of the various forms of retinitis, but as a rule, it is either circumscribed or diffuse. In the former it makes its appearance near the disc, in the shape of a cloudy swelling which radiates along the course of the vessels; vitreous opacities are present. The nerve head is cloudy, of a yellowish red color, the edges are indistinct, the arteries are practically normal, while the color of the veins is darker, there is exudation along the lines of the vessels (perivasculitis). In the latter form the entire retina is edematous and grayish in color, and throughout the retina, and especially near the macula, grayish spots are present.

In syphilitic retinitis, hemorrhages into the retina are rare, though they may occur. The disease generally occurs in from one to two years after the infection; one eye may be affected, but as a rule both eyes are usually involved, but not simultaneously. About 8 per cent of luetics develop retinitis (Alexander). Whereas iritis is rare in other forms of retinitis, it is by no means uncommon in the specific varieties, and likewise iridocyclitis is apt to occur.

The prognosis depends upon the early beginning of appropriate treatment, and even then the condition may lead to one of total atrophy of the nerve.

The ophthalmoscopic signs are: dustlike opacities in the posterior portion of the vitreous, cloudiness of the retina around the disc, which is more or less hyperemic, perivasculitis of the retina and choroidal vessels, numerous isolated yellowish or white spots of exudation beneath the retinal vessels throughout the choroid which follow the same course as in disseminated choroiditis, ending in atrophy.

The subjective symptoms are: vision diminished, flashes of light, night blindness, metamorphosia, scotomata and contraction of the visual field.

Retinitis pigmentosa and retinitis proliferens, at times, have as their etiologic factor, syphilis.

OPTIC NERVE

This structure may be affected throughout its entire course, or any part of it may be the seat of the inflammatory process. The intracranial portion, according to Uhthoff (quoted by Parsons) is affected most commonly, for here it may be attacked by gumma, or by extension of gummous infiltration from the meninges, for the neighborhood of the chiasm is a favorite spot for gummous meningitis.

With the statistics at hand, syphilis seems to stand forth as to etiologic factors. Here, as in inflammatory conditions, a differential diagnosis cannot be absolutely made by the ophthalmoscopic picture, although several writers bring out the fact that in papillitis of syphilitic origin there is a very characteristic thickening of the retinal vessel walls. White striae, which are the result of the inflammatory process accompany the vessels out into the retina.

PAPILLITIS

Papillitis, or inflammation of the intraocular portion of the nerve, manifests itself externally by no sign except that the pupils are dilated in proportion to the diminution or absolute loss of vision. The ophthalmoscope reveals the following picture: increased redness of the disc, the margin becoming indistinct owing to the swelling of the disc, which gradually shades off into the surrounding retina. The retinal vessels are altered; the arteries are smaller than normal, and may or may not be tortuous. The veins are dark, distended and tortuous, especially so when they dip down from the swollen papilla into the retina. Hemorrhages are of frequent occurrence, situated on the nerve head, or in the surrounding retina and generally of a fan-shaped character. The vision may or may not be affected.

CHOKED DISC

Although tumors of the brain are by far the most frequent cause of this condition, yet syphilis cannot be disregarded. The disc is immensely swollen, protruding out into the vitreous like a mushroom; the color is of a glossy grayish red. The arteries are small, while the veins are immensely distended and tortuous, resembling a bunch of angle worms. Occasionally hemorrhages are seen in the disc. The surrounding retina appears normal. The swelling of the disc is primarily due to edema.

RETROBULBAR NEURITIS

Externally the eye shows no symptoms, save the dilation of the pupil, which is in proportion to the defect of vision. The patient complains of central scotoma, and usually there is pain upon movements of the eyeball. The ophthalmoscope first reveals nothing pathognomonic, but in later stages there is hyperemia of the disc, the arteries appear small, while the veins are engorged. The condition is one of interstitial neuritis, which is apparently located in the intraorbital portion of the nerve.

ATROPHY OF THE OPTIC NERVE

In from 40 to 50 per cent of cases of progressive primary atrophy, tabes is the etiologic factor, hence it behooves us to investigate for other symptoms of this disease. The ophthalmoscopic signs are: a bluish white appearance of the papilla, the lamina cribrosa is visible, the margins of the disc are sharply defined. The excavation which is shallow extends to the margin of the disc. Both veins and nerves are smaller than normal. The patient complains of a gradual decrease in vision. The fields of vision for colors are first affected in the following relations: green, red, blue, and white.

OCULAR MUSCLES

Syphilis is by far the most frequent cause of paralysis of both the extraocular muscles and, now that the etiology of tabes has been definitely established by Noguchi, it is safe to estimate that it is the etiologic factor in at least 75 per cent of all cases.

The seat of the lesion producing ocular paralysis may be cortical, nuclear, fascicular, basal or orbital.

Lesions of the cortex, with the exception of ptosis (Duane), never cause paralysis of individual muscles, conjugate paralysis being the result of such lesions. Lesions on the floor of the fourth ventricle, produce, as a rule, paralysis of several muscles; generally it is bilateral. Fascicular lesions, as a rule, cause oculomotor paralysis of the same side with paralysis of the extremities of the opposite side. Basilar lesions, as a rule, affect various nerves in succession as those supplying the ocular muscles, the facial, the olfactory, the trigeminus, the optic nerve, etc. The orbital lesions, the muscles and nerves are usually affected mechanically and are diagnosticated by symptoms indicative of affection within the orbit, such as pain produced by pressure on the eyeball, protrusion of eyeball, monocular optic neuritis, etc.

Argyll Robertson pupil is that condition in which we find that the pupil fails to contract to light, but does to convergence and accommodation. It is quite frequent in tabes. Usually it is bilateral, but it may be unilateral.

With regard to the seat of the lesion, de Schweinitz says, "It has been placed in the fibers which pass through from the proximal end of the optic to the oculomotor nuclei by some authors, and by others it is considered to be nuclear."

TREATMENT

All cases of syphilitic involvement of the eye should be under intensive general treatment in connection with whatsoever local treatment each particular inflammation demands. Only the local will be touched upon in the following paragraph.

In keratitis it is important to keep the iris well dilated to prevent synechia from forming. Atropia 1 per cent should be used every two hours, hot applications every two hours, and the eyes should be protected from light by the use of dark glasses. In the late stages of keratitis, dionin is of aid in clearing opacities. In iritis by far the most important drug for local treatment is atropine, 1 per cent of which combined with 1 per cent of cocaine should be instilled in the eye every two hours. This treatment should be continued until all ciliary congestion disappears. In order to alleviate as much as possible the dryness of the tract produced by atropine, it is well to compress the tear duct after instilling the drug. In retinitis and optic neuritis protection of the eyes from light and absolute rest from all use is requisite.

Section 17

Syphilis of the Ear

SYPHILITIC INFECTION OF THE EUSTACHIAN TUBE AND MIDDLE EAR

As might be supposed from a knowledge of the histology of the part and the all-pervading nature of the syphilitic poison, infection of the middle ear occurs in all degrees and in all stages of the disease, in which an extension through the tube is the most easily understood means when such a tubal lesion exists. Where this causes a catarrhal swelling and tumefaction of the tube, the clinical picture in the middle ear is no different from that of a simple infection, such as retraction of the drum, which is congested, reduced hearing, and possibly a negative Rinné. In early syphilis one of the most constant signs is reduced bone conduction. It can be stated positively that there is no characteristic appearance of the drum, or any definite clinical aspect in a case under the foregoing circumstances. If inflation does not give immediate relief, then we have to deal with something beyond the middle ear; infection of the labyrinth, with or without syphilis of the central nervous system. While it is not susceptible of proof, and is somewhat a matter of academic interest it seems reasonable to suppose that the mucosa of the tympanum is subject to the eruptive conditions found elsewhere in the secondary stage. Here the infection may be catarrhal, adhesive catarrhal or suppurative (Politzer), but, again there is no typical picture to justify the diagnosis of syphilitic origin, as this can be established only after the rapid destruction of the membrana tympani and the marked shortening of the bone conduction. The occurrence of a simple suppurative otitis media complicating a syphilitic infection is not frequent, but the course of the suppuration is relatively so much less malignant and the effect of specific treatment is so little evident in the ear condition that the differential diagnosis soon becomes apparent. The appearance of tinnitus, vertigo and severe loss of hearing should suggest a deeper invasion than that of the middle ear, though both may coexist. All the foregoing conditions are readily submissive to energetic, early treatment in most cases, but when delay has allowed destruction of the drum, entirely or in part, ossicles or any part of the tympanic walls is bad; in fact, Bell's palsy is one of the likely results.

The responsibility of tertiary syphilis for any suppuration in the middle ear is even more difficult to establish than that of the secondary period, yet when it does occur the destructive changes are rapid and extensive.

SYPHILIS OF THE INTERNAL EAR

Auditory disturbances of syphilitic origin usually appear in the late secondary or early tertiary period, though Politzer reports two cases which show the wide range within which hearing may be affected after exposure.

Owing to the insidious nature of the infection and to the usually somewhat casual nature of the aural examination (if, indeed, any be made at all), this complication, as before remarked, has escaped record very often; so the frequency with which auditory disturbances complicate constitutional syphilis cannot be estimated with any satisfactory degree of accuracy. With West, I believe that 5 per cent is sufficiently near the proper proportion to serve as a guide in study and investigation.

The early writers were almost a unit in their conviction that the labyrinth was the part affected in syphilitic disease of the internal ear. Nonne puts his finger on one of the most significant and important facts, hitherto unknown or regarded as negligible, when he comments on the coincidence that frequently disturbances of the acoustic nerve are associated with similar disturbances of other cranial nerves. This observation paves the way to the recognition of the revolutionizing nature of the statement of Swift and Ellis, who have shown rather convincingly that sudden deafness in the presence of syphilis is rarely due to any infection of the eighth nerve, or labyrinth, alone, but is generally a manifestation of the very serious disease, syphilis of the central nervous system, of which more will be said later. In his review of the literature, Benario seems to prove that the eighth nerve is oftener affected in early syphilis than any other cranial nerve.

Sudden loss of hearing, generally with tinnitus, no pain, no evidence of middle ear disease, in a young adult otherwise healthy should be regarded as almost certainly indicative of syphilitic disease of the eighth nerve labyrinth. The high-toned forks will be those least appreciable, and the watch, acoumeter and Galton whistle will elicit little, if any, response, yet conversation may be heard. However, in the marked shortening of bone conduction we have one of the most striking and reliable evidences of luetic infection, as it is perhaps the most common sign, occurring in 95 per cent of the cases. A deafness without apparent middle ear trouble showing a positive Rinné should at once arrest the attention of any aurist.

Section 18

CONGENITAL SYPHILIS

Inasmuch as it is now generally believed that the child which suffers from syphilis at birth is really infected in utero, it is obvious that the expression "hereditary syphilis" must fall into disuse and that the term congenital syphilis is the correct one.

In dealing with the subject of congenital syphilis much trouble will be avoided if we remember that congenital syphilis is caused by an infection with the same organism that is found in acquired syphilis, and that the results of this infection are very similar. For this reason it is possible to write concerning the symptoms and pathology of the disease at a much shorter length.

INFECTION

It is usually believed that the prenatal infection is placental in origin, in spite of the fact that various observers have been able to produce specific lesions in animals by the injection of seminal fluid. It is very difficult to imagine that a sperm cell infected with a treponema could have sufficient vitality to fertilize an ovum. It is likewise difficult to imagine a treponema riding into an ovum astride the tail of a male cell. However, the question is not entirely settled; certain clinical observations made by Williams, Fordyce, and others would seem to indicate that exceptionally syphilis might be paternal in origin.

This is really an extremely practical point. If a wife become pregnant by a man known to be in the early stages of the disease and herself remain free from infection, should she be actively treated so as to treat the child in utero? The answer to this question is doubtful, but inasmuch as arsphenamine will do no harm, the probabilities are that she should be.

Formerly it was taught that when a nonsyphilitic mother, or a mother showing no evidence of syphilis, bore a child suffering from congenital syphilis, she was henceforth immune from the disease (Colles' law). This law is no longer held valid, because it has repeatedly been found that such mothers almost invariably show positive Wassermann reactions. It was also formerly believed that when a healthy child was born of a syphilitic mother the child could not acquire syphilis. This was known as Profeta's law. It has also been found that such children very frequently show positive Wassermanns, hence are in all probability suffering from a latent form of lues.

SYPHILIS OF THE PLACENTA

Correa-Dias, Schwab and Williams have shown that a syphilitic placenta is much larger than a normal one. Frankel called attention to the changes in the chorionic villi in 1873. When they are teased out in salt solution they are seen to have become much thicker and more club-shaped than is normal. Microscopically there are characteristic syphilitic changes in the blood vessels, and the stroma cells are closely packed, instead of being stellate. Plass has recently confirmed these findings.

FREQUENCY

It is a well-known clinical fact that by no means all syphilitic parents bear syphilitic children. Every syphilographer realizes how frequent it is to have under his care a man who has acquired syphilis ten or fifteen years before, who has had a totally inadequate course of treatment, and yet who has children that show neither the clinical nor the laboratory signs of syphilis. In many instances this can certainly be explained by the fact that the mother of the children has remained unaffected. Just what percentage of children born of syphilitic mothers are affected is as yet uncertain. However, certain it is that when a woman has active syphilis it is unusual for her to bear healthy children. One of the most marked effects of syphilis upon the fetus is the interruption of pregnancy; it is rare to find a syphilitic woman who has not had from one to five miscarriages. Kassowitz states that over 40 per cent of pregnancies result in miscarriages. Lynch and McInnes have emphasized the importance of syphilis upon the resulting fertility of the women, and my hospital experience has been identical with theirs. It is frequently noted that the first pregnancies following a syphilitic infection are prone to result in miscarriages, the next child may be born dead, and that the next child may die soon after birth. In other words, the children conceived soon after infection have a much worse immediate prognosis. In my own experience about 3 per cent of all syphilitic patients seen in private practice are affected with the congenital form of lues, while in dispensary practice the figures run between 8 and 10 per cent. It is certain that many more cases would be seen if it were not for the fact that there are so many miscarriages and so many early deaths.

CLINICAL COURSE

Many authorities divide congenital syphilis sharply into two great groups, that group showing early manifestations, and that group not showing lesions until after the age of puberty. Fournier has directed particular attention to the latter, calling it syphilis hereditaria tarda. In reality while this classification may be useful clinically, yet pathologically it is analogous to acquired syphilis, for as has already been emphasized it is not unusual to find that after a very mild early course severe late lesions may develop after the lapse of many years.

For years it has been the custom to blame various malformations in the child to the effects of syphilis. For instance flat foot, scoliosis, and various other of the bone deformities, congenital heart disease, hernia, deaf-mutism, malposition of the viscera and many other troubles have been laid at the door of syphilis. Now as a matter of fact a child is syphilitic or not syphilitic, and it is extremely improbable that any of these dystrophies are caused by lues.

It is usual for the syphilitic manifestation to appear shortly after birth; ordinarily the child when born appears healthy. Miller in a study of one thousand cases noted that the time of the appearance of lesions was as follows:

First week,	8.5	per cent
Second week,	13.8	“ “
Third week,	24.0	“ “
Fourth week,	17.7	“ “
Second month,	22.0	“ “

The lesions seen early in the course of congenital syphilis do not differ materially from those seen in the same stage of acquired lues. There is usually an eruption, mucous patches, some glandular enlargement, condylomata and frequently a marked alopecia upon the back of the head where it has rubbed upon the pillow. However, there are a number of other features that must be considered. There is usually more systemic disturbance than is found in the acquired type of the disease; the child rapidly becomes poorly nourished and is frequently very fretful. Very often there is a marked rhinitis that gives rise to ‘‘the snuffles.’’ The face often looks pinched and there may be rhagades from the corners of the mouth. A little later gummous changes may develop in any organ. The bone changes may develop from those occurring in acquired lues and will later be described in detail. Dactylitis is more common. At times there will be no early manifestations noted and gummata will be the first lesions observed, they rarely appearing before the child is two years of age.

EARLY CUTANEOUS MANIFESTATIONS

A pure macular type of eruption is rather uncommon, but nevertheless may occur. More commonly the lesion is either maculopapular or distinctly papular. While many of the authors speak of the maculopapular lesion as being the most common, it seems to me that they are really referring to the discoid papular type, for as a rule there are white scales upon the lesions, a finding that does not occur in the true maculopapule. While this eruption may be generalized as in the acquired types it is not infrequent to find that the lesions are more circumscribed. They have a special tendency to occur upon the buttocks and around the diaper region. Upon the palms and soles there may be an erythema with a slight amount of scaling that is not absolutely characteristic but which is extremely suggestive. In some exceptional instances there may be a generalized, mildly exfoliating dermatitis. As a general rule, however, the eruption is very similar to that already described in the section upon early cutaneous manifestations.

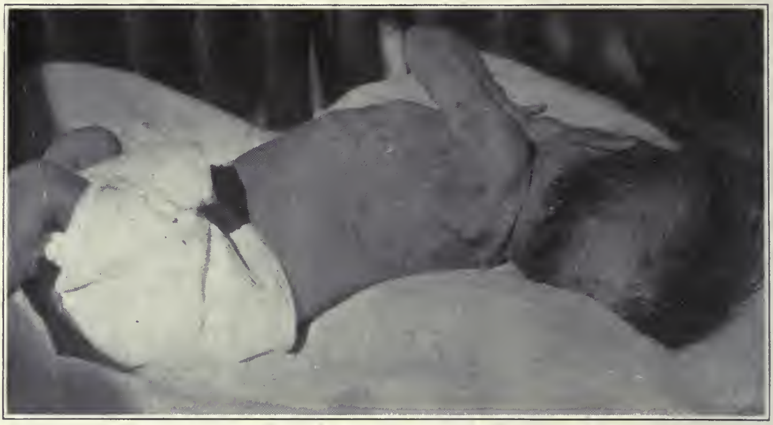

Fig. 46.—Children suffering from congenital syphilis not infrequently show a maculopapular eruption, together with a few superficial ulcerations.

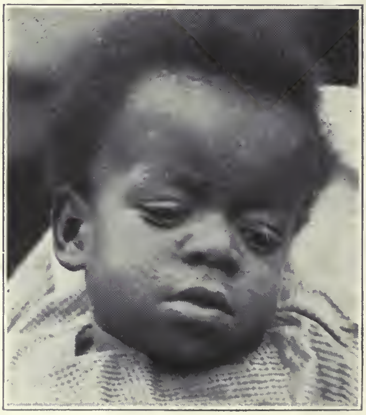

Fig. 47.—Annular lesions may be found in the negro children suffering from congenital syphilis. (Courtesy Dr. E. P. Copeland.)

Lenticular papules are uncommon but at times do occur. In the negro typical annular lesions may appear upon either the face or body.

Superficial pustules are extremely rare, but it is not unusual to find a few scattered ecthymoid pustules. Again these resemble those found in acquired syphilis.

Vesicular lesions are rare, although they may occur in connection with bullous lesions. Grindon has recently described two cases. According to him Rollett was one of the first to describe this condition, and Crocker, Adamson, Taylor and others have described cases. The vesicles may be either generalized or localized, and vary in size from one-twelfth to one-third of an inch. While the lesions are usually closely grouped, nevertheless they do not coalesce as in eczema.

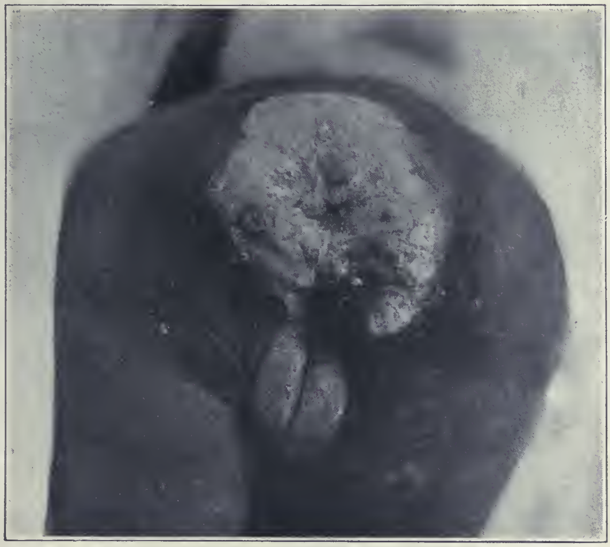

Fig. 48.—Large superficial lesions may develop about the anus, and are at times called "giant condylomata."

Bullous lesions, the syphilitic pemphigus, are not as common as the majority of text books would have us believe. In over three hundred cases of congenital lues I have encountered this condition but twice. The bullae are most common about the hands and feet and the adjacent portions of the limbs, but may occur upon any portion of the body. In size they may reach well over an inch.

They may be either distended or flaccid, and the contents may be either clear or cloudy. The base is usually raw. They are frequently surrounded by an inflammatory areola. Such lesions must be distinguished from both pemphigus and bullous impetigo, and the clinical diagnosis may depend upon finding other manifestations of syphilis, usually not a difficult procedure.

Condylomata are frequently found about the perineum and anal region, and may reach a very considerable size.

LATE CUTANEOUS MANIFESTATIONS

As a general rule it may be stated that the late cutaneous lesions of congenital syphilis are comparable to the lesions developing in the course of late acquired syphilis. However, the gummous lesions are the most common. It is rather unusual to see the serpiginous nodular lesions that are so often encountered in the acquired type of the disease. The destruction resulting from ulcerating gummata is often very extensive, and the lesions may be extremely intractable to treatment according to the statement of most syphilographers. Squamous syphilides of the palms and soles are very rare.

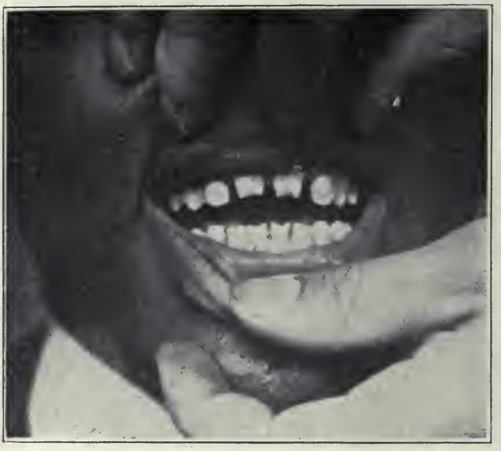

Fig. 49.—The notching in Hutchinson's teeth is characteristic.

AFFECTIONS OF THE MOUTH AND THROAT

Mucous patches are extremely common in congenital syphilitics. They are identical with those affecting persons with acquired syph-

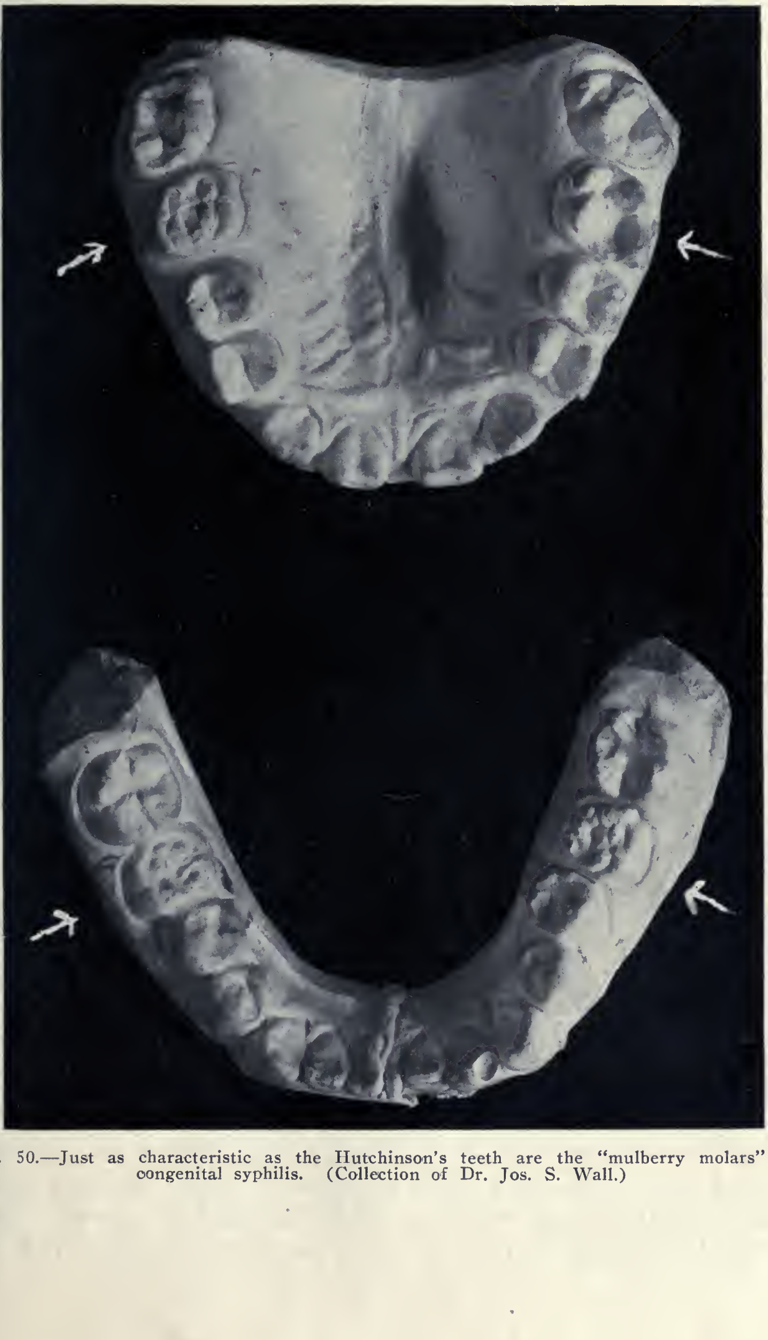

Fig. 50.—Just as characteristic as the Hutchinson's teeth are the "mulberry molars" of congenital syphilis. (Collection of Dr. Jos. S. Wall.)

ilis. The other lesions occurring within the mouth are to all intents and purposes identical with those already described. However, special attention must be directed to the teeth, for here are found certain characteristic changes.

In children suffering from congenital syphilis the teeth are frequently late in erupting.

The typical "Hutchinson's teeth" of congenital syphilis are the upper middle incisors of the second or permanent set. Typical teeth have a single central notch in the center; the tooth is usually small both in length and width, and is not flattened out as is normal, but is frequently rounded or peg-like.

Dr. Jos. S. Wall (Arch. of Pediat., October, 1917) has recently called attention to very important changes which occur in the six-year molars. He has found that these teeth show changes much more regularly than do the central incisors, and that the changes are even more characteristic. To quote Wall: "There is an erosion, not the erosion of wear only, but a disintegration of the grinding surface, to which this term is applied in the absence of a better one. This erosion is irregular in form; the surface of the molar for a third or half or even the whole surface is pitted, excavated and discolored. There is often a pulpy mass of dirty yellow color occupying most of the face of the crown, margined, as it were, by the line of cusps ordinarily found on the molar teeth. The tooth has been called the 'honey-combed molar of hereditary syphilis.' We have spoken of it in our clinics as the 'mulberry molar,' likening the worm-eaten center of the cutting surface to the appearance of the tip of a mulberry."

In regard to syphilitic lesions of the throat it is only necessary to say they are similar to those of acquired syphilis.

AFFECTIONS OF THE HAIR AND NAILS

In some few cases of congenital syphilis the hair may grow very rapidly and be very dark in color, and has been designated by Hutchinson as the "syphilitic mop." Still says that this has occurred in four per cent of his cases. Still further says that in six per cent of his cases there has been a marked alopecia, especially over the vertex. In a number of hospital cases I have seen a complete baldness upon the whole back of the scalp, and am inclined to believe this to be rather common. The hair of the eyebrows may be lost as well.

AFFECTIONS OF THE RESPIRATORY SYSTEM

Syphilis of the Nose.—Diday supposed that syphilitic coryza was due to the presence of mucous patches within the nose, but such is not now believed to be the case. Frequently shortly after birth it is noted that the child develops a coryza or "snuffles." This is a purulent rhinitis, that frequently becomes offensive. The child has a peculiar snorting inspiration, and frequently holds the head back to aid in respiration. Suckling is always interfered with. Still claims that coryza is present in 70 per cent of the cases. The upper lip often becomes eroded, and the mucous membranes of the nose may become permanently atrophied. This form of syphilis does not lead to saddle nose, which is always due to gummous changes. The gummous lesions are in no wise different from those of tertiary acquired syphilis.

Syphilis of the Larynx.—Still claims that 14 per cent of his cases showed hoarseness. This may be due either to a simple inflammation or to actual ulceration. These children may have attacks of laryngeal spasm, and some "crowing" is frequently observed.

Syphilis of the Trachea and Bronchi.—Connor in his excellent review of the literature upon this subject found 10 cases of congenital lues as opposed to 118 cases of acquired form. The symptoms are the same in either form of the disease.

Syphilis of the Lungs.—The best known condition is the pneumonia alba, found in stillborn children, and which was first described by Virchow.

It is probable that there are mild degrees of this condition which are consistent with longer life and in which there are pathologically fibroid changes in the interstitial tissue.

Gummata are usually considered rare, but Still, Behrend and Barlow have reported cases. The symptoms are comparable to those already discussed in the chapter on acquired syphilis of the lungs.

SYPHILIS OF THE DIGESTIVE TRACT

Syphilis of the Salivary Glands.—There are but five cases reported in the literature. Haslund has recorded one early in life where there was an acute inflammatory swelling. The other four cases were gummata that occurred late in the course of the disease.

Syphilis of the Esophagus.—Wile's excellent article upon esophageal syphilis makes no mention of the congenital type of the disease, although he reviews the literature very thoroughly. It is probable that cases have escaped recognition.

Syphilis of the Stomach.—So far only pathologic reports of congenital gastric syphilis are available. These have been made by Chiari, Flexner, Gaillard, Buttner and others. All agree that either the whole stomach wall or merely portions of it may be involved, and that usually it is involved throughout its entire thickness. Miliary gummata, with syphilitic changes in the vessels and some diffuse infiltrations, are found.

Syphilis of the Intestines.—While congenital syphilis of the stomach seems to be rare, that of the intestines is much more frequent, although all of our reports come from the autopsy room. Councilman has reviewed the reports of Kundrat and Mrazek, Baumgarten, Wagner and Chiari. He states that the lesions are usually found in the small intestine, but that they may occur in the large. In general there are two forms, one where only the Peyer's patches or solitary glands are involved and one where the disease is scattered irregularly throughout the whole of the small intestine. The histologic findings are similar to those occurring in the stomach. At times there may be an adhesive peritonitis. Other cases have been reported by Fraenkel and Buttner.

Syphilis of the Liver.—Rolleston gives an excellent account of congenital syphilis of the liver. Gubler first described the disease in 1852. Lancereaux gives an admirable historical review of the subject. Hepatic syphilis is extremely common in congenital syphilitics, Hofmeister putting the figures at 39 per cent and Feige at 65 per cent. Rolleston considers that there are three main types, that occurring at the same time that the secondary manifestations appear, the tardive type, and the multilobular cirrhosis that supervenes in later life. In the first type the child may be born healthy and the lesions develop rapidly, or the child may be stillborn. There are usually signs that point to liver disease, such as an enlarged liver, although jaundice and ascites are frequently absent. The liver is firm and tender: at times there is a localized tumor formation, but this is rare. The spleen is frequently enlarged as well. When jaundice does occur it may be due to secondary infection as Milon has pointed out. Pathologically the changes are usually diffuse: the surface may show adhesions, but usually the surface is smooth. On section it is firmer than normal, and there is some mottling due to some portions being more affected than others, there being yellowish areas. Small gray spots are usually to be distinguished; these are small gummata. Microscopically there is a proliferation of the connective tissue elements, and of the endothelium of the capillaries and lymphatics inside the hepatic lobules. Characteristic changes around the larger vessels are usually to be made out. As a late stage it is found that the individual liver cells may be separated one from the other by proliferated fibrous tissue. Still later there may be well-marked bands of fibrous tissue that traverse the organ.

When the hepatic changes do not occur until a late date they are comparable to those of late acquired syphilis. The disease is not very rare: cases have been reported by Wilks, Morris, Fournier, Hudelo, Forbes, Mackenzie and others. Lardaceous changes frequently complicate the picture.

The parasyphilitic multilobular cirrhosis is not a result of the ordinary pericellular cirrhosis so common in early life. The multilobular cirrhosis usually comes comparatively late after birth, often not for many years. The clinical features are those of portal cirrhosis in children, namely portal obstruction, ascites and wasting.

Syphilis of the Gall Bladder and Gall Ducts.—There are no cases upon record of syphilitic involvement of the gall bladder. However there are two cases of congenital stenosis of the ducts due to syphilitic deposits, those of Beck and Rolleston.

Syphilis of the Pancreas.—There are upon record numerous cases of specific involvement of the pancreas in congenital syphilitics. Oser gives an admirable review of the subject. He states that Birch-Hirschfeld found changes in 23 cases, and that out of 124 cases the pancreas was involved in 27 instances.

Hecker also found similar changes in 22 per cent of his cases. A chronic indurative pancreatitis was the lesion usually found, but miliary gummata have also been described. Klebs has found frank gummata. Marshall has suggested that a pancreatitis due to syphilis may be the cause of some cases of diabetes found in the young.

SYPHILIS OF THE VASCULAR SYSTEM

Syphilis of the Pericardium.—But little is to be found in the literature upon syphilitic pericarditis. It is true that gummous processes may extend through from the myocardium and Wanitschke has shown that they may also extend from the mediastinum.

Syphilis of the Myocardium.—Syphilitic lesions of the myocardium have been well described by Warthin, on a basis of fifty cases that he had studied. He divides the lesions into parenchymatous and interstitial, just as in the cases of acquired cardiac syphilis. Treponemata are frequently found either in the tissue spaces of muscle, or about the blood vessels, without any demonstrable lesions. Pale degeneration of the heart muscle is also found. At times fatty degeneration or simply atrophy occur.

Other observers have reported the presence of true gummata in the heart muscle of congenital syphilitics.

Endocarditis and Diseases of the Valves.—The literature has but little to say in regard to syphilitic endocarditis; however, in view of the immense number of organisms in a child with congenital lues it seems certain that the endocardium cannot escape damage in all cases. In view of the well-known fact that congenital syphilitics suffer from specific arteritis they must at times have aortic insufficiency. Anders calls attention to this fact.

Heart Block.—Nanta and Saundby have both reported cases of heart block developing in persons suffering from congenital syphilis.

Arteritis.—Typical syphilitic aortitis may be induced by the treponema in congenital syphilis, as Klotz has shown. As a result of these, aneurysm may develop as both Le Boutillier and Osler have emphasized.

Raynaud's Disease.—It has already been pointed out that there is great confusion in the literature as to the differentiation of Raynaud's disease from arteritis, especially syphilitic arteritis. Cases of so-called Raynaud's disease in persons suffering from congenital lues have been reported by Hutchinson, Marsh, Humphrey, Duckworth, and many others. Lisser has recently added another case and given a complete bibliography.

Syphilis of the Veins.—Thompson states that the veins in those suffering from congenital syphilis are often weak, and that marked dilatation of the superficial veins of the scalp is often noted in young infants. I have seen several instances of severe forms of angiomata in the syphilitic negro, in whom angiomata are very rare.

Syphilis of the Blood.—It is a well-known fact that there is often a marked secondary anemia in connection with congenital lues. Chiaravalloti has examined the blood of 150 cases and found that the hemoglobin varied from 12 to 75 per cent, with a corresponding decrease in the number of red blood cells. It is usually stated that a high lymphocyte count is the rule, but I have been unable to confirm this finding, only one of my five cases showing a high count.

Syphilis of the Spleen.—That syphilis of the spleen is common in congenital syphilis has been recognized since the publication of Gee's paper in 1867. In 1877 Barlow confirmed this observation. Coutts found the spleen enlarged in 62 out of 100 cases, and Still states it is easily palpable in 45 per cent of the cases and at least one inch below the costal margin in 22 per cent. There are three types of lesion, the simple hyperplasia, the diffuse fibroid changes, due of course to miliary gummata, and the true gummata, examples of which have been reported by Still and others.

Syphilis of the Lymph Glands.—It is generally considered that the superficial lymph glands are not so constantly enlarged in congenital syphilis as in acquired syphilis, a point with which I agree thoroughly. However, during the early stages it is usually possible to find a number of such glands, and in almost every case I have found that the epitrochlear glands were palpable. This at times may be a valuable diagnostic point. True lymphomata have been reported by Still, Holt, and others.

SYPHILIS OF THE BONES, JOINTS, MUSCLES, TENDONS AND BURSAE

In general it may be said that the lesions of the bones, joints, muscles, tendons and bursae in congenital syphilis are very similar to those occurring late in the acquired form of the disease: however there is one lesion that is characteristic of congenital lues, namely osteochondritis.

Syphilis of the Bones.—While osteochondritis (epiphysitis) is unquestionably the characteristic osseous lesion of congenital syphilis, still periostitis and osteitis do occur and not rarely. Dactylitis is also fairly common.

Periostitis may occur at practically any stage of the disease and is in reality a counterpart of the type found in the acquired form, although there may be rather more deformity. The tibiae are probably more frequently affected than are any of the other bones, and the well-known ''sabre tibiae'' may result, they being due to a marked convexity of the anterior edges. The usual course of the disease is for the subperiosteal gummata to calcify, but ulceration to the exterior may result.

Osteitis and osteomyelitis are similar to the condition already described in the chapter on acquired syphilis of the bones. However, the skull bones are not so frequently affected, while the nasal bones are more frequently involved.

Parrot has described bossing of the skull as due to lues. A typical text book case should show four thickened, rounded elevations at the vertex of the skull surrounding the anterior fontanelle: at times, however, only two are present. Coutts believes that four bosses indicate syphilis, but Still cannot concede this point. Rickets may give a similar condition.

By craniotabes various observers mean various conditions; some mean simply a diffuse yielding of the edges of the parietal bones on pressure, while others limit the term to islands of parchment-like bone surrounded by well ossified areas. In either condition Still believes that rickets is the most frequent cause, despite the opinions of Barlow and Lees, who reported 47 per cent as due to lues and Carpenter who considered 74 per cent as luetic.

Dactylitis is not infrequent. Still gives an incidence of 2 per cent. In the vast majority of instances it occurs before the age of two is reached. The proximal phalanges of the fingers are usually affected, but the toes may be involved, and in one or two cases the metatarsals have been affected. Clinically there are usually several fingers involved, and the disease may be uni- or bilateral. A fusiform swelling slowly develops and it is unusual for this to soften or break down. The condition is due to periostitis, epiphysitis and to osteitis or osteomyelitis. It must be distinguished from tuberculosis, and the age of the patient, as well as the various clinical and laboratory signs will aid in making a correct diagnosis.

Osteochondritis was first described by Wegner in 1870. Many men have written on the subject, but one of the best descriptions is that by Post. According to this observer three types of lesion occur. The most characteristic and typical occurs along the line of ossification; the single line of demarcation becomes thickened and enlarged. In advanced stages a subluxation may occur. In addition there is frequently some periostitis, and also certain changes in the marrow, which may be responsible for the anemia that sometimes accompanies congenital lues. Osteochondritis frequently results in the stunted growth of the long bones. The pseudoparalyses of Parrot are not infrequent accompaniments of the disorder. Usually there is considerable tenderness on pressure and the child cries when handled. This form of osseous syphilis is far from uncommon. Still states it occurs in from 11 to 22 per cent of all cases.

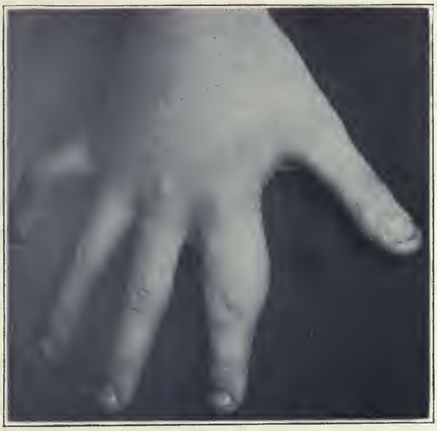

Fig. 51.—Children frequently show dactylitis. (Collection of Dr. Richard L. Sutton.)

Syphilis of the Joints.—Lesions of the joints in congenital syphilis are far from rarities as is proved by the figures of the following authors: Dunlop had 16 cases, von Hippel reported joint lesions in 56 per cent of his cases, Still in 7 per cent. Males are more apt to be affected than are females. The following classification may be adopted: arthralgia, synovitis, hydrarthrosis, osteochondroarthritis, gummous synovitis, osteoarthritis or von Gies joint.

Arthralgia naturally cannot be well recognized in young children, but tenderness on pressure may give a clue. Fournier thinks that it is rare, while the majority of other authors do not mention it.

Synovitis or pseudorheumatism is not mentioned by the majority of authors, but occurs in much the same form as in acquired syphilis.

Hydrarthrosis was first described by Clutton and frequently goes under the name of "Clutton's joints." The majority of writers upon congenital joint lesions now recognize them as distinct types of congenital arthritic syphilis. These joints usually develop in early adolescence: the only sign or symptom is the presence of fluid in the joints. The knees are most frequently affected and the effusion is frequently bilateral. The synovial membrane is the site of diffuse gummata. Treatment is usually prompt in its results. It has been suggested that recovery is more rapid if the fluid be aspirated under aseptic conditions.

Osteochondroarthritis is especially well described by Gouriantz. This author states that it is fairly frequent and usually appears between the ages of 8 and 13. The lesions are frequently bilateral and the joints are affected in the following order of frequency, knees, elbows, hips, and ankles. The onset is insidious, claudication being the first symptom; this is due to deformity from epiphyseal hyperostosis and effusion. The effusion is clear. The synovial are swollen and present plaques upon their surfaces, but there are no fungus growths. When the lesion becomes advanced the joint is globular in shape, the skin is thinned and shows a network of blood vessels. There is no local adenopathy and no contractures or deformities.

Gummous synovitis is very similar to the type occurring in the acquired form of the disease.

Osteoarthritis or von Gies joint was first described by this author in 1881. It occurs later in the course of congenital lues than do the other types described above. The condition is a multiple, progressive chondritis or chondroarthritis. Its pathology is not dissimilar to that of the atrophic arthritis of Goldthwaite. The cartilage of these joints is thinned and ulcerated, frequently leaving small islands of cartilage in an otherwise denuded end of bone. The epiphysitis is soft, and the remaining cartilage is soft and friable. The joint membranes are covered with villi, which resemble the fat pads in the ordinary types of arthritis deformans. The bone itself frequently shows other syphilitic changes. It is rather difficult for the authors to sharply differentiate this type of arthritis from osteochondritis on the one hand and from Mericamp's type of syphilitic arthritis deformans on the other. In fact there is probably no hard and fast dividing line between the conditions, and they are rather examples of degree than of any essential pathologic difference.

Syphilis of the Bursae.—Churchman, in his extensive review of luetic bursopathies, states that there are no undoubted cases of congenital syphilis of the bursae in the literature but that there are several suggestive cases, which he cites fairly fully. Since this time Coues has reported a case, which, however, is not absolutely beyond criticism.

THE KIDNEYS IN CONGENITAL SYPHILIS

In early as well as late congenital syphilis, specific lesions of the kidney occur usually in association with specific lesions and congenital deformities of other organs and parts of the body. All varieties of nephritis are met with, but as a rule the kidney changes are overshadowed in importance by other manifestations of the disease. An exhaustive study of the subject may be found in the monograph of Karvonen.

Early Congenital Syphilis of the Kidneys.—Among certain of the earlier authors affection of the kidneys in congenital syphilis was considered rare (Lancereaux, Polnow, Spiess). Klebs in 1876 stated that intrauterine kidney syphilis is apparently not so rare as it appears, but is generally overlooked. Fournier states categorically that kidney diseases are common in congenital syphilis, "an undeniable fact as shown by hundreds of observations."

Symptomatology.—As a rule there are few or no symptoms referable to the kidney.

The following pathologic changes are described by Karvonen: arrested development; parenchymatous nephritis; kidney hyperemia; interstitial nephritis; and gumma.

Late Congenital Syphilis of the Kidneys.—According to Fournier and Karvonen, under this heading grouped (1) cases in which the symptoms appear first after several years and (2) cases in which early congenital syphilis run their course and after a long latent period appear in a new form. While a number of cases have been reported, our knowledge of the subject is still very rudimentary and uncertain.

SYPHILIS OF THE FEMALE GENITALS

Vulva.—Condylomata of the vulva are not uncommon during the florid stage of congenital syphilis. They are usually associated with an eruption upon the other portions of the body, and with condylomata of the perineum.

The vagina, cervix and body of the uterus are not affected according to the reports of Gellhorn and Ehrenfest.

Fallopian Tubes.—Doenhoff has reported the case of a new born child who died from congenital lues. The tubes were thickened throughout their entire length. Microscopically they showed syphilitic changes. Ballantyne and Williams have reported a similar case.

Ovaries.—There are no records concerning syphilitic disease of the ovaries. However, according to Gellhorn and Ehrenfest treponemata have been demonstrated in the ovaries by Hoffmann and Wolters, Levaditi and Savage, Bab and others.

SYPHILIS OF THE ENDOCRINE GLANDS

A considerable number of cases of luetic involvement of the endocrine glands have been reported. Unfortunately in most of these cases we have only pathologic findings and no clinical history, due to the fact that the lesions were discovered at autopsy. For a general discussion of the subject the reader is referred to the chapter on acquired syphilis of these glands.

The Thyroid.—It is usually stated that congenital syphilis of the thyroid gland is rare, but this may be because it is not looked for. Demme states that he has seen children with gummous nodules, and Gombault, Garnier and Clark have reported cases. In Clark's patient there were marked symptoms of hypersecretion, no exophthalmos, pulse rate two hundred, palpitation and extreme nervousness. Under specific medication recovery occurred.

The Parathyroids.—No literature upon this subject can be found.

The Thymus.—Adami states that both gummata and diffuse fibroid changes may be found, and Hochsinger believes that there may be a very marked enlargement which subsides under therapy. Possibly the Dubois abscess has aroused more interest than any other lesion. Chiari holds that this is a cavity lined by epithelium, and derived from accumulation of the cells within a Hassal's corpuscle, but Simmonds and Schlesinger think that the cyst formation is due to arrest of development of some of the epithelial tubules that give rise to the thymus. Warthin has suggested that in some cases it is due to postmortem softening of the gland. Weisel has given a complete bibliography of the subject and Oliver has written a good article.

Pancreas.—Syphilis of the pancreas has already been discussed.

Testes and Ovaries.—Lesions of these organs have been discussed elsewhere.

Suprarenals.—Syphilitic lesions of the suprarenals have been found at autopsy, but the symptomatology is practically unknown. Cases have been reported by Esser, Kokubo, Vmogradoff, Simmonds and others. In a late paper Simmonds states that the most frequent pathologic change is the so-called perihypernephritis syphilitica, the process being in the capsule and associated with atrophy of the cortex. In addition gummata and necrotic areas frequently occur in medulla.

Pituitary.—Lancereaux states that the pituitary may be enlarged and indurated in congenital syphilis. Simmonds was able to collect ten cases from the literature, those of Simmonds, Schmidt, Chiari, Triboulet, Dalpy and Hardwick. Also it is probable that syphilitic disease of the pituitary can, either directly or through internal hydrocephalis, cause the adipose genital dystrophy of Bartels.

In addition it is certain that various glands may be diseased at the same time, so that various symptom-complexes result. Reede tells me that he has seen a number of such cases in congenital syphilitics which he is as yet unable to classify satisfactorily. Vagli has also called attention to this fact.

CONGENITAL SYPHILIS OF THE NERVOUS SYSTEM

In congenital syphilis the nervous system is involved in 13 per cent of all cases, according to Rumpf. In America examination of the spinal fluid has given a somewhat higher percentage. The symptoms are most apt to appear about the time of puberty.

Practically all the forms of nervous syphilis which are discussed elsewhere (see Chapter on Syphilis of the Nervous System) can occur in children, showing essentially the same symptomatology so that it is not worth while to repeat these descriptions here. The most common forms are juvenile paresis and juvenile tabes. There are, however, other affections of the nervous system due to congenital syphilis which are not met with in the adult forms, such as certain forms of feeble-mindedness, hydrocephalus, ependymitis, Friedreich's ataxia, primary optic atrophy, Little's disease, a nervous form of rickets, simple nervousness, and amaurotic idiocy. Pure spinal syphilis is, according to Nonne, never found in congenital lues.

Hydrocephalus is comparatively frequent in congenital lues. Syphilitic arteritis is the usual cause of this malformation. There is an exudation of lymphatic fluid in early intrauterine life causing a watery accumulation in the ventricles. Hochsinger has studied 35 cases. The usual time of onset was from the third to the eleventh month. Six cases began in the uterus. Eleven cases showed no nervous symptoms. The symptoms are disturbances of consciousness, mydriasis, myosis, vomiting, bradycardia, convulsions, paresis and muscular rigidity. Cases have been reported cured by antisyphilitic treatment.

Other brain conditions, such as ependymitis, may occur in congenital lues. The syphilitic toxin, transmitted from the parent to the fetus, comes in contact with the developing nervous system and causes the deformities of malformations. Brain apoplexies may occur, arteritis, or disease of the meninges. The optic nerve is frequently involved in hereditary syphilitic basilar meningitis.

Occasionally a symptom-complex develops which resembles closely Friedreich's ataxia. The differentiation may be impossible and depends on the spastic symptoms, convulsions, and paralyses of the eye muscles.

In congenital syphilis a rachitic nervous picture may appear so that these children from slight causes develop eclamptic convulsions. The pathology of this is hard to explain.

Sachs described a series of cases of idiocy which he did not suspect arose from syphilis. Such cases of amaurotic idiocy usually occur in several members of the same family; postmortem they show disease of the cells, and medullary fibers of the cortex. Spastic paralysis of the extremities may occur together with the dementia and in some cases vision fails progressively, resulting finally in blindness.

The prognosis in congenital syphilis of the nervous system is on the whole bad. So many of the cases are those of defective development or malformation of nervous tissue, giving rise to anomalous functions, that we cannot expect any improvement. Even in those cases where the symptoms are acquired, if we may use that term, the attack of the virus on the nervous system is usually so severe or has progressed so far before recognition that there is enormous destruction of nerve tissue which cannot be replaced.

The treatment does not differ from that of the same symptom-complexes in the adult. The juvenile paresis is just as hopeless, if possible more so—the juvenile tabes has the same prognosis under treatment. Early diagnosis and energetic treatment are the two main points. Psychic disorders in the juvenile form yield but little to treatment. The youth of the patient, beyond a certain point, has proportionately little bearing on the dosage of the spirocheticides employed. It is required that the nervous tissue be sterilized as far as possible and this cannot be done by handling the case gingerly.

CONGENITAL SYPHILIS OF THE EYE

Lesions of the deep structure of the eye are by no means of infrequent occurrence in congenital syphilis of infancy and young children; especially is this the case in diseases of the uveal tract. The iris is of the plastic type and differs in no essential points from that of the acquired type, save in the time of its appearance, and the fact that the symptoms are usually slightly marked.

It is usually bilateral and generally associated with cyclitis or choroiditis. The time of its appearance is stated by various authors as about the fifth month, although cases occurring during the first month have been reported.

According to Weeks, gummous iritis may appear at any time after six weeks, but seldom after the age of thirty.

Choroiditis is by no means uncommon in infants and young children and, as it presents no external signs, usually it is not discovered until the individual is of sufficient age for the vision to be tested. It presents the same ophthalmoscopic picture as the acquired type.

Lesions of the retina and optic nerve, like those of the choroid, give no outward signs of their presence, therefore are only recognized when an ophthalmoscopic examination is made, and for this reason, it is indeed essential that infants of parents in whom syphilis is known to exist, should be subjected to a thorough ophthalmoscopic examination at frequent intervals until grown.

The optic neuritis of infancy and children is generally associated with a choroiditis. The papilla is indistinct and hyperemic and usually there is no edema of the disc, and in many of these cases atrophy of the optic nerve follows sooner or later.

Paralyses of the extraocular muscles, especially the internal muscles in children, are usually traceable to congenital syphilis. Ingersheimer brings out rather an interesting fact that in twelve cases of nystagmus in young children with negative ophthalmoscopic findings and vision practically normal, the Wassermann reaction was positive in eight cases.

Undoubtedly some forms of congenital cataract are of syphilitic origin, in so much that they may be the result of a syphilitic involvement of the uveal tract in utero, therefore, it is essential to search for the other stigmata of lues in these cases. Fine dust-like vitreous opacities, especially of the anterior portion, in young children is quite indicative of syphilis due to a preexisting inflammation of the uveal tract, and great care should be taken in searching for the other signs of syphilis.

Interstitial keratitis is the most common symptom of congenital syphilis in children between the ages of five to sixteen, although it may appear earlier. It is looked upon as essentially of congenital origin, yet, at times, it is seen in the acquired type. The disease usually begins gradually with slight ciliary congestion followed by the appearance of one or more faint cloudy patches usually near the center of the cornea. Upon examination these are seen to be within the corneal structure. These gradually spread and fuse until the entire cornea becomes lusterless and dull. Blood vessels derived from the ciliary vessels begin to make their appearance in the corneal structure, producing a dull yellow appearance, giving rise to the characteristic salmon patch. After the disease has reached its height, it begins to subside, the cornea clearing from the margin towards the center and finally becomes clear again, except in severe cases. Sufficient treatment with arsphenamine will effect a cure, despite reports to the contrary.

Iritis is always associated with interstitial keratitis and occasionally choroiditis and retinitis. The disease is bilateral and whereas the second eye may become involved shortly after the first, yet as much as a year has elapsed before it has made its appearance. The subjective symptoms are diminution of vision, pain, lacrimation, and photophobia.

Various opinions have been advanced as to the true pathology of interstitial keratitis. Parsons considers it an extension forward of a choroiditis, while others claim that the infiltration is due to the direct action of the treponemata, and yet others are of the opinion that it is due to the toxins.

SYPHILIS OF THE EAR

West's division into three groups of congenital syphilitic disease is a rational method for study, as the clinical features are so different in each of the three, and inasmuch as they occur at such widely different ages. The following in his classification: (1) Cases showing gross aural disease at birth; (2) cases showing aural disease shortly after birth, (3) cases showing aural disease at or after adolescence, or much later (i.e., all cases not included in Classes 1 and 2).

Of the lesions of the external ear, seemingly due to congenital syphilis Dabney has seen three cases of microtia. Fortunately for society and their own happiness most of the children showing gross syphilitic disease die shortly after birth, but in those less frequent instances where they survive, they become not only deaf mutes, but often mental defectives as well.

The hopeless nature of the prognosis in labyrinthine cases is easily grasped in a perusal of Baratoux's investigations. Of 43 cases reviewed, 19 were stillborn, but of the 24 surviving, 8 had chronic suppurative otitis media, 3 isolated labyrinthine disease and 8 both middle ear and labyrinthine disease. The labyrinthine cases showed either suppuration therein or hemorrhage and destruction of Cort's organ. The suppuration in this second group may be nonspecific in rare instances, but even so, its course is affected necessarily by the lowered vitality, and rapid destruction of the drum and tympanic contents is apt to ensue, even the internal ear being penetrated by the suppurative process in extreme cases.

The frequently encountered type of congenital aural disease is that of the adult and late life. According to West the proportion of congenital syphilitics who have deafness and other aural manifestations of syphilis is thus dated by various observers: Hutchinson and Jackson 10 per cent; Hermet and Baratoux, 30 per cent (Politzer); Habermann, 20-66 per cent; Aly, 3.1 per cent (labyrinthine deafness); Hinton, 5 per cent (all seen at Guy's Hospital). There is a little closer agreement than this among the authorities as to age limits, eight to eighteen years, this being the general estimate, or in the neighborhood of fourteen years.

In the appearance of interstitial keratitis we have presented to us not only a diagnosis of the aural condition impending, or actually active, but a warning as well that treatment started at this time will probably heal in part any aural lesion, but also energetically persisted in will probably prevent those parasyphilitic lesions, which are so destructive to the health and economic value of the patient, even to life itself. The keratitis nearly always precedes by days or weeks the lesions, though it may develop simultaneously with it. As the symptoms of the adult congenital syphilis of the ear are almost the same as those of acquired labyrinthine syphilis there is no need to repeat them.

DIAGNOSIS

The clinical diagnosis of congenital syphilis is usually not difficult to make. In young children several things must be looked for. The history is always important. The parents may give either a history or evident lesions of lues. A history of miscarriages is always of much importance. In the child itself several points must be noted: the general condition is frequently below par, the child may have a wizened appearance and the face may look like that of an old person. There may be rhagades from either the mouth or the anus. An eruption is common. "Snuffles" are frequent, although it must always be borne in mind that rhinitis is frequently found in children who do not have lues. The joints may be painful. Enlarged epitrochlear glands are frequent, and other enlarged glands may occur. The spleen is enlarged in a high percentage of cases, and the liver is often even larger than usual.

In older children frank gummata may occur. Hutchinson has called attention to a triad of symptoms, namely, deafness, interstitial keratitis and Hutchinson's teeth. Periosteal lesions should be looked for.

In regard to the laboratory diagnosis but little need be added to the chapter upon general diagnosis in acquired syphilis. It is not always easy to obtain blood for a Wassermann. If it cannot be drawn from a vein in the arm either the external jugular or a scalp vein should be tried. These veins always become engorged when the child cries. If the blood cannot be obtained directly from a vein either a puncture or a slight incision may be made in the skin and the blood collected from this. The Wassermann is of extreme value in congenital lues for it is usually positive in the florid stages, although not always in the late stages. Unfortunately most of the articles do not state in what stage of the disease the patient is. Craig states that he has had 82.2 per cent of positive reactions. Holt states that the reaction is practically always positive, and Veeder and Jeans found 92.2 per cent of eighty-two positive. Noguchi gives the results of some other observers in his book. It is generally believed that in syphilis hereditaria tarda a positive reaction is the rule, but in view of the fact that in late acquired syphilis the test is not frequently negative it is extremely probable that this cannot be the case.

In newborn children the best way to make the diagnosis is by microscopic examination of the umbilical cord.

PROGNOSIS

It has long been recognized that syphilis is a frequent cause of intrauterine death. Kassowitz states that out of 330 cases only 40 per cent reached term. Still states that in the families of 87 congenital syphilitics there were 39 stillbirths and 36 miscarriages. Post has studied 168 pregnancies and found that there were 53 stillbirths and miscarriages. Hyde after an elaborate study found that in seventeen hundred pregnancies there were 579 abortions and stillbirths.

Two recent articles are particularly important. Williams found that over one-third of all fetal deaths were due to syphilis; in other words that syphilis ranks highest among the causes of fetal death. White and Veeder in a very careful study report that syphilis is responsible for 21.7 per cent of miscarriages and stillbirths in syphilitic families.

As to the after history of children with congenital syphilis there is a pretty fair agreement in the literature. Osler states that about 75 per cent die. Hyde says that out of 1121 born alive 956 died within the first year. Sturgis reports that in Moscow from 63 to 82 per cent of the affected children succumbed. Still says that out of 87 cases there were 25 cases attributable to congenital lues, and that thirteen more died while under observation. According to Post out of 115 children there were 44 early deaths, and 32 more showed later lesions. Kassawoitz reported that 34 per cent die within six months, while Eteinne has estimated that 95 per cent die if untreated, and 10 per cent if treated.

A more recent paper based upon modern thorough therapy, and using the Wassermann reaction as a control, has recently been published by White and Veeder (Amer. Jour. Syph., 1922, vi, 371). Of 197 cases less than two years of age the mortality was a trifle over 20 per cent. For their total series of 443 cases the mortality was nearly 18 per cent. Breast-fed children did much better than bottle-fed infants. Syphilitic children were more prone to fatal results from intercurrent infections than were nonsyphilitic children. Children over five years of age had the same mortality rate as nonsyphilitic children. The results in general were discouraging; they considered but 22 per cent as cured and 35 per cent as improved. These poor results, of course, are frequently due to the fact that it is impossible to give adequate treatment. Unquestionably there should be legislation compelling the parents of a syphilitic child to give it every chance for recovery.

As regards the individual prognosis there are a number of distinctly bad signs; these are an eruption present at birth, severe pemphigus, jaundice, early nerve lesions and inability to digest food.

PROPHYLAXIS

There are three ways to prevent congenital syphilis: first, to prevent the marriage of syphilitics; second, to prevent conception in a family in which one or both of the partners have the disease, and third, to intensively treat the syphilitic pregnant woman. The first of the points will be covered in the Chapter on Prophylaxis, and the second need not be here discussed. However, the question of the effective treatment of the pregnant must be gone into in some detail. There is considerable literature upon the subject. Jeanselme observed fourteen cases that were treated with arsphenamine and mercury and concludes that the former is superior and that the child will usually go to term and be born alive. Sbilinsky gave arsphenamine to a patient in early pregnancy and two hours later there was hemorrhage with abortion. Auderbert treated seven pregnant women with arsphenamine and most of the children were born healthy and remained so. Two of the cases were confined prematurely. Bar has reported upon six cases which he treated with neoarsphenamine; he was convinced that the drug might be dangerous. V'Scilly treated ten patients and found that all gave birth to healthy children. Sauvage has treated 130 women with arsphenamine. He reported that the blood pressure was somewhat raised and felt that this fact should make one cautious in administering the remedy. In 3 out of 84 cases the arsphenamine seemed to hasten the time of birth. Thirty-eight women came to labor at the natural extreme limit, 32 bore their children at the ninth month, two in the eighth, and two in the seventh. The fetal heart sounds became weaker after the administration of the preparation. Of the 91 children, 84 were born living, 77 showed no signs of syphilis after birth, and only 5 were known to have developed syphilis. Pinard, de Ribes, Boissard and Patocki treated 217 cases by mercury or potassium iodide. In 74.54 per cent the children were born dead and in 10 per cent they later developed syphilis. One hundred sixty-three cases were treated with arsphenamine. Over 66 per cent of the children were born alive and without signs of syphilis, 15 per cent showed syphilis soon after birth and the remainder were born well ahead of time and were dead. Other reports quoted by Davis, who has written a complete article upon the relation of syphilis to obstetrics, show that arsphenamine is much the better drug. In our own hospital work we never hesitated to give arsphenamine to pregnant women and so far have had no occasion to regret it. Because of the class of patients with whom we have dealt it is impossible to say just what the results have been.

TREATMENT

Before discussing the treatment of children with congenital syphilis it is well to consider the pathologic condition. In children who show signs of lues soon after birth it must be remembered that the treponemata are already diffused through all of the organs and that they are usually present in great numbers. In other words, the condition is similar to that of a well-developed secondary stage of acquired syphilis, except that there are probably more organisms present. In the late stages there are not so many organisms, but the body is in a state of allergy. In other words, it is probably impossible to ever produce a radical cure such as can often be obtainable in the early stages of acquired syphilis.

It is extremely important to look after the general health of children suffering from congenital syphilis. If possible they should be breast-fed rather than bottle-fed. They should be carefully protected from acquiring any acute infectious disease. An abundance of fresh air and sunlight is essential.

There have been many men who have tried to treat nursing children through the media of their mothers. However, the results have not been good as Englemen, Doblin, Baisch, Ascheim and others have pointed out.

It is probably always necessary to treat the child direct with either arsphenamine or mercury. The iodides have no value in killing the treponemata, and are upsetting to the digestion, hence are no longer used. Mercury may be given by the mouth, but care must be taken not to disturb the digestion. Either the protiodide or mercury with chalk may be used. Of the latter we use from ½ to 1 gr. three times a day. One-sixth of a grain of the protiodide a day for a young child is sufficient. The most popular form of administering mercury is by means of the inunctions. The blue ointment, ung. hydrar. fortior, is the old favorite. About one dram is rubbed over the binder nightly, and the binder then wound around the infant's body. This should be removed daily and the body washed. Intramuscular injections are favored by some, but in general they are irritating and not to be recommended. If one is to use them the best of soluble salts is certainly the succinimide, employed in doses of $\frac{1}{40}$ of a grain two or three times a week, or the biniodide dissolved in sodium iodide, the dosage being given according to weight, and employed but once a week. Neither of these preparations is especially irritating.

Turning to arsphenamine and neoarsphenamine we find that in the early days a number of deaths were reported from both preparations, and it was thought that the killing of a large number of treponemata and the freeing of their toxins into the circulation might be responsible. Of late we have heard but little of this view.

Older children should have arsphenamine administered by the intravenous route. Young children may receive it in three different ways: either intramuscularly, intravenously or into the longitudinal sinus.

The dose by the intramuscular route should be given from once in ten days to once in two weeks, and the greatest of care should be taken that it be injected into the muscle and not into the subcutaneous tissue. The upper and outer quadrant of the buttock is a suitable site for injection. Either neutralized arsphenamine or neoarsphenamine may be employed. It is possible that sulfarsenol, a French preparation which is similar to neoarsphenamine, may give less trouble when injected intramuscularly than do other preparations, but I wish to most emphatically state that this has not as yet been proved, although a recent article by Voeghtlin, Dyer and Thompson (Am. Jour. Syph., 1922, vi, 526) would seem to indicate this possibility. The dose should be graduated according to the weight of the child. Infants weighing 15 pounds should receive one-tenth of the adult dose, that is 0.04 grams of arsphenamine. If neoarsphenamine or sulfarsenol be employed the dose should be just twice that of arsphenamine. I have had considerable experience with the Hynson, Wescott and Dunning preparation of arsphenamine in cocoa butter and it has worked very well. Fordyce and Rosen are firm believers in the intramuscular route, and I also have had excellent results from it. On the other hand White and Veeder claim to have a great amount of pain as a result. This, I have never seen; although I have seen abcesses where one injection was given into an area of induration or where some of the substance was allowed to leak into the fat.

In employing the intravenous route it is usually preferable to elect a vein in the elbow. In certain cases a vein on the front of the scalp may be easily accessible. Many workers prefer the jugular vein, but this is thin walled and subject to sudden collapse from changes in intrathoracic pressure so that it is very easy to either miss the vein or to run the needle through both walls. Personally, I prefer the use of a syringe and a needle of from 20 to 22 gauge. The expert can easily administer arsphenamine to almost any child over 8 months of age. The dosage is the same as for the intramuscular injection and intervals of about a week are usually employed.

The use of the longitudinal sinus is mentioned only to be condemned. It is not difficult to produce an infiltration in the brain substance which may end fatally. Although the literature contains very few references to this subject, still I know of a number of cases where death has ensued.

In all cases of congenital syphilis the treatment must be long continued; practically never less than 2 years of almost continual medication. Alternating courses of arsphenamine and mercury should be employed as will later be indicated under the treatment of late syphilis. The physician should never be disturbed because the Wassermann fails to clear up promptly.

ARGYRIA AND ITS RELATION TO SILVER THERAPY

I. Argyria—Historical. II. Retention and Elimination of Silver with Special Reference to Silver Salvarsan and Silver Therapy

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THE use of silver in modern therapy occasionally has caused some alarm on the part of the clinician, due to the possibility of producing an intoxication whose outward manifestations have been designated by dermatologists as argyria. Argyria (argyrism, argyrosis) is the term applied to a pigmentation or permanent discoloration of the skin which sometimes follows continued or prolonged administration of silver or silver salts due to an absorption and ultimate deposition of silver or a silver compound in the tissues and cutaneous surfaces. This discoloration may even be extended to other surfaces such as the conjunctiva, the buccal mucous membranes, and the urethral tract.

Argyria was once a very common form of intoxication which followed the prolonged use of silver nitrate and certain colloidal silver preparations; at present it is comparatively rare in spite of the extended application of silver compounds in therapy. The first case of argyria was reported by Angelus Sala (1647) using silver nitrate internally in the treatment of epilepsy. The second case of argyria was seen in 1791 by Schwediauer and reported by Fourcroy. Early in the XIX Century, on account of the extensive use of silver in the treatment of epilepsy and tabes, many cases were reported and it would not be surprising to find many cases at the present time in instances where the old form remedies are still in use.

Argyria may be classified in two main groups which may be called "generalized" and "localized" pigmentation. The generalized group invariably will have its pigmentation produced as a result of internal medication and absorption in which the blood is involved: whereas the localized group is composed of metal workers and those patients who receive local applications on the buccal, urethral, and conjunctival mucous membranes. In every case which is involved in this report, the pigmentation has been the result of the treatment with ionizable silver compounds or the deposition of metallic silver in various areas through mechanical means or the use of colloidal silver. In local argyria the silver penetrates directly into the skin or by way of the mucous membrane and the discoloration never goes beyond the place of application.

The application of silver compounds in modern medicine has been very widespread and in this class of drugs are found the simple ionizable compounds inorganic in nature; the simple colloidal preparations, the organic silver derivatives, and more recently the complex coordination compound called silver salvarsan. The recent work of Ballenger and Elder (1922) is well worth discussing in this connection inasmuch as these authors bring out the phagocytic action of the drug whose activity is due to definite germicidal emanations, an idea quite new to the use of silver chloride. The work of Cobb (1921) also has an important bearing on this particular point. Cobb employed " 'a solution of an ordinarily insoluble substance rendered soluble by extreme subdivision, i.e., the particles must be smaller than $100\mu\mu$ or less than $\frac{1}{250,000}$ of an inch.' To better realize the actual minuteness of colloidal particles it can be illustrated by the fact that approximately a million of them could be put into the space occupied by one red blood corpuscle or ten thousand into one gonococcus, were it a hollow sphere." This product possesses properties of being nontoxic, nonirritating and free from any staining quality.

In order to arrive at a definite idea of the action of this type of drug, it has been necessary to study the literature and the case reports concerning the matter, so that the type of drug causing these disturbances can be compared with the theory advanced, the biochemical results found, and the pathology developed.

It has appeared wise to go into the case reports somewhat in detail in order to dissipate some illusions which gradually appear, and likewise to clarify the relation of silver to argyria.

The discussion of cases in chronological order will be found first. This will be followed by the theories for absorption. The animal experiments will then give the results of an extended study. These animal experiments will be further clarified by a detailed quantitative pathological study of the animals in question.

From a study of the literature it appears that localized argyria is not much more prevalent than the generalized. After a careful review of the literature, *thirty-six* cases of localized argyria have been reported since 1857. In two instances the authors stated that there were several other cases. *Forty-four* cases of generalized argyria have been reported, the first case being the one pointed out by Angeles Sala in 1647. In addition there is the alleged case brought to the attention of the medical profession in 1920 by Lochte who did not actually see the case.

''The case mentioned by Lochte was found, on investigation, not to have been seen by him at all but was mentioned by him on the strength of a report made by a 'naturopath.' Regarding the authenticity of this report, Dr. Scholl, Hoechst on Main, states in a letter dated Dec. 2, 1920:

''In the above mentioned publication Lochte makes a brief statement in which he cites references placed at his disposal by the 'naturopath' regarding a case of supposed argyria after silver salvarsan injections and, using this case as a basis on his own behalf, cautions against the use of such products. Lochte expressly denies the authorship of the sensational heading 'Argyria after Twelve Silver Salvarsan Injections,' and states that the case report as sent to him bore this heading. Further, he states that he himself has not seen the case, although he requested that the patient call on him. He accordingly was not in a position to confirm the diagnosis of the naturopath, and he himself suggests the possibility of an arsenical melanosis.''

Sollmann (1918, p. 780) states: ''The inorganic silver salts, especially the nitrate, are used to produce astringent, caustic and antiseptic effects. They form resistant precipitates with proteins, so that their local action is easily controlled. The toxicity for higher animals is very low, and the antiseptic efficiency is high. In the presence of the tissues, silver surpasses mercury, since the protein compounds of silver are also antiseptic. These may be used directly when antiseptic action without irritation is desired.

''Silver is not absorbed in sufficient quantity from the alimentary canal to produce systemic actions. Because of its precipitation by proteins and chlorid, even large doses of silver nitrate rarely produce serious poisoning. Long-continued use results in blackish discoloration of the skin (argyrism) by the deposition of silver particles, probably organic. Traces must therefore be absorbed.

"Argyrism.—This develops gradually after prolonged internal or external use of silver when the total dose has reached 15 to 30 gm. Since silver is now rarely used in this way the condition is infrequent. It has been produced by the application of silver-containing hairdyes. Argyrism consists in a bluish-black discoloration of the skin, especially where exposed to light; and of internal organs and mucous membranes (Frommann, 1857; Riemer, 1876). The black granules do not consist of metallic silver, for they are easily soluble in KCN, and difficultly in concentrated nitric acid. In the skin, they are situated in the connective tissue of the corium, and remain indefinitely. No silver can be demonstrated in the urine. The argyrism does not give rise to other symptoms. In animals, silver deposition has also been produced in internal organs, but not in the skin.

"Systemic Actions.—These are never seen in man but may be produced in animals by the injection of nonprecipitant silver solutions (AgCl in sodium thiosulphate, Gaehtgens, 1890: colloid AgCl or AgI, Gros, 1912). The actions are mainly on the central nervous system, consisting of paralyses and spasms beginning in the lower extremities; disturbances of respiration; and fall of blood pressure (paralysis of vasomotor center ?); sometimes diarrhea. The secretion of bronchial mucus is greatly increased, probably by injury to the epithelium, and may lead to asphyxia. Death occurs usually promptly, by paralysis of respiration; the diaphragm being paralyzed before the other respiratory muscles. The heart is but little affected and may beat after death. In frogs, the paralysis is preceded by convulsions (Ball, 1865; Jacobi, 1877; Gaehtgens).

"Chronic systemic poisoning shows changes in the blood corpuscles; disturbances of metabolism; cloudy swelling of the heart and skeletal muscle; and fatty degeneration of the liver and kidney (Bogoslowsky)."

With this introduction it is of interest to tabulate the cases of argyrism that are available in the literature. It is true that many cases will be omitted through failure to report and also due to the

TABLE I

GENERALIZED ARGYRIA (CHRONOLOGICAL ORDER)

DATE	OBSERVER	DRUG	DOSAGE	SEX OF PATIENT	METHOD OF APPLICATION	DISEASE AND SITE OF APPLICATION	PERIOD OF DEVELOPMENT COMMENT
1647	Angelus Sala	$AgNO_3$		1 case			
1791	Schwediauer	$AgNO_3$		Male	Internally	Stomach	
1843	Graham	$AgNO_3$		1 case			
1845	Krahmer	$AgNO_3$		1 case			
1851	Hebra	$AgNO_3$ (?)		2 cases			
1859	Frommann	$AgNO_3$	1½ gr. daily, 7 days. 6 gr. daily	1 case	Internally	Stomach	9 mos.
1874	Duguet	$AgNO_3$		2 cases	Internally Painting	Pharynx	
1875	Riemer	$AgNO_3$		Male	Pills, internally	Stomach, Tabes	1 yr.
1878	Neumann and Weichselbaum	$AgNO_3$		Male	Internally	Tongue, stomach disorder	20 yrs.
1879	Liouville	$AgNO_3$		1 case	Internally		
1883	Tweedy, H. C.	$AgNO_3$	⅓ gr. daily	Male	Internally	Tabes	12 yrs.
1884	Dittrich			1 case			
1887	Schallenberger	$AgNO_3$	⅓ gr. daily	Female	Internally		2 yrs.
1887	Walters	$AgNO_3$		Female	Painting throat	Swallowed some	Many yrs.
1888	Foote	$AgNO_3$	Solid	Male	Painting throat	Swallowed some	8 yrs.
1889	Onodi	$AgNO_3$	10%	2 Male		Gangrenous larynx	years
1895	Crusius			Female	Externally	Varicose veins	
1895	Tweedy, see Tweedy 1883						
1895	Zieger	$AgNO_3$		Female	Externally	Varicose veins	2½ yrs.
1899	Menzel	$AgNO_3$		Male			
1905	Lewin and Guillery	$AgNO_3$	500 gr. (total)	Male	Internally	Tabes	
1906	Allen	$AgNO_3$	⅕ grain	Female	Internally, pills	Stomach trouble	5 yrs.
1907	Heuter	$AgNO_3$		Female	Internally		
1909	Weber	$AgNO_3$	¼ grain	Female	Internally	Gastric sympt.	2 yrs.
1911	Gottheil	$AgNO_3$	10-15% daily, 3 times	Male	Internally	Throat	5 yrs.
1914	Crispin	Collargol		Female	Internally		¾ yr.
1917	Steiger	$AgNO_3$	4 grains Ag in 7 mos.	Female	Internally	Multiple sclerosis	
1917	Steiger	$AgNO_3$		Male	Internally	Tabes	4 yrs.
1917	Nobl	$AgNO_3$		Male	Internally	Syphilis	
1920	Cohen	$AgNO_3$		Male	Internally	Indigestion	7 yrs.
1920	Smith	$AgNO_3$	¼ grain 3 times da.	Male	Internally		3 mos.
1921	Barthelemy	$AgNO_3$	Consumed 144 gm. $AgNO_3$ in 15 yrs.		Internally	Tabes	18 mos.
1921	Goldstein	Argyrol	Twice daily	Male	Internally	Throat	1 yr.
1922	Kimball	$AgNO_3$		Male	Internally	Duodenal ulcer	Consumed 1 oz. Ag.

42 Cases of Generalized Argyria specifically mentioned.

TABLE II

LOCALIZED AND INDUSTRIAL ARGYRIA (CHRONOLOGICAL ORDER)

DATE	OBSERVER	DRUG	DOSAGE	SEX OF PATIENT	METHOD OF APPLICATION	DISEASE AND SITE OF APPLICATION	PERIOD OF DEVELOPMENT COMMENT
1857	Junge	First Histological exam.		Several		Conjunctiva	
1872	Ollivier	Ag		Female	Industrial	Hands and face	
1878	Lewis	Ag		Male		Conjunctiva	
1880	Knies	$AgNO_3$	Every other day, 40-50 yrs.	Male		Eyes	
1886	Lewin	Ag		Male	Industrial	Hands	Out of 700 gold and silver workers, 218 had spots
1886	Blaschko	Ag		Male	Industrial	Localized	Silver workers
1886	Blaschko	Ag		Female	Industrial		Several workers
1887	Ensor	$AgNO_3$	3 times daily, for 3 days	Male		Conjunctiva	
1887	Gruenfeld	$AgNO_3$ sol.		Male		Urethra	
1888	Grossman					Conjunctiva	
1893	Olshausen	$AgNO_3$		Female	After burns	Gums, cheeks, etc.	
1893	Kobert	Ag		Male	Industrial		
1899	Hoppe	$AgNO_3$	¼% sol. 6 yrs.			Conjunctiva	
1903	De Schweinitz	Protargol	1 yr.			Conjunctiva	
1905	Chatterton	Argyrol	5% drops daily for some time	Male		Conjunctiva and skin	
1905	Chatterton	Fulminate of Argyrol		Female	Industrial	Conjunctiva and skin	
1905	Post	Argyrol		Female		Eyelid, follicular catarrh	
1905	Post	Argyrol		Male		Gonorrhea	
1906	Steiner	$AgNO_3$		Male		Conjunctiva	
1907	Ipsen			Male		Gonorrhea	

TABLE II.—CONT'D.

DATE	OBSERVER	DRUG	DOSAGE	SEX OF PATIENT	METHOD OF APPLICATION	DISEASE AND SITE OF APPLICATION	PERIOD OF DEVELOPMENT COMMENT
1908	Nance	Drops	3 times a day for more than 4 weeks	Female		Conjunctiva	
1908	Larkin	$AgNO_3$		Female		Conjunctiva	
1909	Hirschberg	Ag		Male	Industrial	Eyes, darkened	Silver polisher
1909	Krause	Argyrol	25% daily for 4 mos.	Male		Conjunctiva	
1909	Krause	Argyrol	20% daily for 20 mos.	Child		Conjunctiva	
1911	Gabrieledes	Ag. photo plates		Male	Industrial, photographer	Skin	Licked silver surfaces
1911	Gabrieledes	$AgNO_3$, Protargol	20 yrs.	Female		Conjunctiva	
1911	Harman	$AgNO_3$		Female		Conjunctiva	
1911	Harman	$AgNO_3$		Child		Conjunctiva	
1911	Landesberg	$AgNO_3$		Male		Painted throat and larynx	
1911	Schwarz	Silver dust $AgNO_3$					No. of cases not given
1912	Alt	Argyrol		Male		Conjunctiva	
1912	Ewing	Protargol		Male		Conjunctiva	
1912	Koelsch	Argyrol and		Female	Industrial		Several cases
1914	Teleky	Ag		2 Male	Industrial, Silver beads		Several cases
1914	Teleky	Ag		Female	Industrial, Silver beads		Other cases reported
1916	Davidson	Argyrol Protargol (Albargin)	800 gr., 10% 200 gr. Total equiv. to 400 gr. Ag.	1 Male		Urethra	6 weeks to develop
1917	Olson	Argyrol				Conjunctiva	
1917	Steiger	$AgNO_3$			Brush applications	Conjunctiva	Trachoma
1921	Beeson	$AgNO_3$		Male		Nose	

fact that the record is not easily available. Personally, one of the authors (M) knows of four cases that are not reported. However, in each instance the causative agent is silver nitrate used as pills either for tabes, gastric ulcer or other stomach disorders. After careful search of the literature and case reports it is apparent that age, sex, and organic disturbances play no well-defined part in the predisposition to the intoxication.

In summarizing the above tables it is apparent that generalized argyria is produced in nearly all of the cases as a result of the use of silver nitrate. In most instances it is brought about by the internal use of the drug either taken for stomach troubles or by accidentally swallowing the nitrate as a result of application in the mouth.

In the table dealing with localized and industrial argyria it is readily apparent that all types of silver compounds of certain structure are causative agents. In this table nitrate of silver, argyrol, protargol, albargin (representing the colloidal silver preparations) and metallic silver dust have contributed to this intoxication. It is observed that the amounts of silver used in this form of intoxication are small. Therefore, it lends no weight against the possibility of producing the generalized type if the amount is increased and the method of application is of such a nature as to produce products easily deposited in the cutaneous surfaces.

Excluding the observations of Lewin (1886) the number of cases of localized and generalized argyria are about the same.

The next questions which arise in the mind of the investigator are the cause of the intoxication and the manner in which it is brought about. In order to arrive at a quantitative estimation of these possibilities the authors of this article carried out a large group of experiments on animals, the results of which are found in the succeeding articles.

Several interesting theories have been advanced explaining the reasons for the intoxication. In studying these theories, the work of Lewin (1880) on rabbits showed that a blue discoloration of the skin was produced after tatooing with fine silver particles. This observation is indicative of the solution of the metallic silver and ultimate deposition of this product in areas acted upon by actinic rays. Tattooing of humans did not reveal the same results (6 cases). Jacobi (1878) studied experimental argyria in rabbits using the subcutaneous injection of finely divided metallic silver, and the administration of various silver preparations by throat. However, all his experiments covered too short a time to give generalized argyria. There was a noticeable discoloration of the intestines with traces of silver in the liver. Loew (1884, 1885) succeeded in proving the possibility of reduction of silver compounds in living tissues of animals. Olson (1917) injected argyrol into rabbits and states that the histopathology is the same in animals as in man. The elastic tissue especially is involved showing fine granules of silver pigment. The epidermis and the epithelium of the sweat and sebaceous glands are very rarely pigmented with silver stain. Huet (1873) fed rats on powdered sugar and silver nitrate using one-half milligram per day for each animal. One animal survived four months, another six months and the two others more than a year without any discoloration of the skin. With these illustrations of animal experiments it is apparent that no satisfactory results can be obtained by waiting for the outside manifestations of the intoxication. Only careful histopathological examination of the tissues will give any idea as to the changes which have taken place. Discoloration of the skin, the conjunctiva, mucous membranes, intestinal tract are easily observed. Silver deposits (Kanitz, 1909) are also found in the glomeruli of the kidneys, the mesenteric glands, the spleen, the liver, marrow of bones, the choroid plexus, lungs, etc. The investigation of Kanitz shows that there is pretty general distribution of silver throughout the body as a result of the argyria.

Archard and Emile Weil (1907) using collargol, observed that the bony marrow was extremely red. Koelsch (1912) did not believe that there was an elimination of silver through the kidneys in spite of a contrary assertion of Charcot. Kino (1909) states that the characteristic pathological, and anatomical indications of argyria universalis are: (1) Silver deposits are found in all organs; (2) they are always extracellular; (3) they consist of such characteristic formative elements, that it is almost impossible for them to undertake a change; (4) they are almost specifically bound to elastic and related substances. Olson (1917) states that the pathology of argyria due to organic silver compounds is very similar to that of argyria due to silver nitrate. The silver pigment shows a specific affinity for the elastic tissue fibers. These fibers contain the granules of silver pigment in combination as elastin silver.

With these facts in mind it is quite apparent that silver compounds capable of producing generalized argyria have a wide distribution through circulation of the blood.

Industrial argyria which is caused by silver dust getting into the skin surfaces needs little discussion. It is probable that small amounts of the metal slowly dissolve in the localized body fluids and then are acted upon by actinic rays which tend to destroy the semisoluble silver complex.

Localized argyria falls in nearly the same category. The insolubility of the new derivative keeps the silver localized whether nitrate or colloid is used. The amount of silver is so small that it would be difficult to produce generalized symptoms. In other words the quantity of drug is so small and the method of distribution so poor that the symptoms usually are restricted to the site of application.

The theories proposed for generalized argyria are that the preparation is reduced to metallic silver in the intestinal tract and the finely divided silver is filtered out in the cutaneous areas and then acted upon by light; another view is found in the idea that the chloride is formed and is deposited in the skin where the usual darkening of silver chloride takes place in the presence of sunlight. Tweedy (1895) expresses the cause in the following manner: (1) The reduction of silver salts administered takes place in the stomach and afterwards in the intestinal canal. (2) The reduced silver finds its way to the organs of the body through the lymphatic passages. (3) It is not eliminated by the urinary organs or by the intestines. (4) It does not, as a rule, produce any material effect upon the health.

Steiger (1917) expresses his views in these words, "Since the silver deposit in the skin is practically a tattooing with an insoluble substance that cannot be absorbed, argyria is beyond our therapeutic resources. The only chemicals which, in theory, could dispose of the silver particles, are strongly toxic."

Foote (1888) states, "Riemer's views with regard to the chemistry of argyrosis are considered most probable. He assumes that silver, having been reduced in the intestine and being in a state of finest subdivision is taken up by the chyle-vessels, transported into the blood-current and then deposited in the various organs.

There is a difficulty in reconciling this view with the undisputable fact of the influence of light on the staining of the uncovered parts for the color of the reduced silver can no longer be altered in any way by the light. Were it found in the tissues as the insoluble chloride, the pigmentation would be very intelligible, as the white chloride is very sensitive to light especially in the presence of organic matter. Postmortem examinations show that the discoloration is not limited to the skin and superficial mucous membranes, but may extend to the liver, spleen, and intestinal mucous membrane. The nervous system seems to be exempt from depositions of silver granules.''

Beeson (1921) states, ''Lewin and Blaschko have observed localized argyria in silver workers. In them minute particles of the metal became detached during the various processes, such as filing, turning and polishing, to which it had been subjected. These tiny foreign bodies apparently penetrated the epidermis lodged in the corium. It was believed that in these cases, just as in those due to ingestion, the silver was first changed into a soluble salt from which it was reduced and then deposited.''

Burdon-Cooper (1907) makes the following statements. ''Several views have been advanced to account for the stain. One, perhaps the most popular, sought the essence of the reaction in the decomposition by light of a hypothetical silver proteid compound but we cannot hold such a theory at the present day, in view of our extended knowledge of proteids; for it has been shown that proteids from which all trace of salt has been removed give no reaction with silver nitrate. It would serve no useful purpose to go into the other theories, suffice it to say that it has now been definitely shown by two quite independent observations that the all important element in determining the stain is the chlorine of the soluble chlorides, which exist so abundantly in the intercellular material of the tissues generally and less so in the protoplasm of cells but which is absent altogether from normal nuclei. It is this chlorine that determines the distribution of nitrate of silver when it is applied to the conjunctiva; and the writer has proved to his own satisfaction by experiments on the penetration of nitrate of silver into colloids (egg albumen, gelatine, etc.) that not only is the distribution influenced by the rate of penetration also, and the latter in such a remarkable way that it can be expressed almost as a law as follows: 'that the rate of penetration of a soluble silver salt into a colloid is, other things being equal, directly proportional to the chlorine in the latter, capable of reacting with the silver salt.' The depth of penetration from similar experiments he has found to be dependent on the strength of the silver solution solely. It is not influenced by the chlorine. For those who are not quite familiar with what happens when nitrate of silver is allowed to penetrate into gelatin or egg albumen it may be said that the precipitated chloride of silver is not deposited uniformly but in layers and Ostwald has explained this by assuming that precipitation begins only when the critical concentration of the advancing solution is reached and continues until the solution is brought back to the metastable condition; when this has taken place another development of the labile condition obtains and thus another stria after an interstriate zone is formed. As the silver salt becomes more and more dilute critical concentration is attained later and later and so new striae are separated by interstriate zones of increasing width. The writer does not pretend to infer that what takes place in these laboratory experiments occurs in a similar manner in the case of a living membrane such as the conjunctiva, but such experiments are suggestive and throw a good deal of light upon the action of nitrate of silver. And the writer believes that something very similar occurs in practice although of course the distribution of the chloride of silver in the conjunctiva is much less regular and uniform than in the case of the gelatin.

"In view of what has been said I had better allude to the seat of the stain at this point. This has been given variously by different observers as in the lymphatics (Stephenson) and elastic tissue (Grossmann). The distribution of nitrate of silver in the conjunctiva is not influenced as we have seen above by the soluble chlorides, which by chemical affinity attract the nitrate along those channels in which the halogen is found in greatest proportion. The extent to which the nitrate obeys this influence is dependent on the strength of the solution applied. In this way, to my mind, the apparent discrepancy between two observations which are both correct in a measure is to be accounted for, as a stain will be produced wherever chlorides exist, but the exact delimitation is a function of the concentration.

"We know that the nitrate which has penetrated into the conjunctiva is then converted into chloride of silver, AgCl. The alteration in color of this on exposure to light, we are all familiar with, how a light brown color changes to dark olive brown which eventually becomes grayish-black. The brown coloration is either a lower chloride of silver (argentous chloride) or an oxychloride, and as to the grayish-black stain that eventually remains, the writer is not quite certain as to whether this is the black oxide of silver or metallic silver; it is usually put down to the latter. The writer has noticed that corneal stains persist longer in the brownish stage than those of the conjunctiva. Why, he cannot say, presumably the difference in the circulation has something to do with it. If the black stain is an oxide then the term reduction staining should cease to be applied to the process of staining by nitrate of silver.

"The bluish-white pellicle which follows the application of nitrate to the conjunctiva is not coagulated albumen as is usually supposed, but chloride of silver deposited in the structure of the membrane which is most likely to be followed by staining. The writer's experience is in favor of drops and the explanation, I believe, is as follows: a strong solution of silver nitrate (15 gr. to 1 oz.) will be precipitated in the cells to such an extent as wholly to destroy their vitality—they are cast off together with the chloride they contain and in this way the greater amount of silver chloride is got rid of. Some nitrate, however, penetrates deeper but the critical concentration after the initial precipitation is insufficient to determine a deposit of chloride in the cells in sufficient quantity to destroy them (weak solution). This chloride undergoes the change above described. It is precisely this incapacity on the part of a weak solution of nitrate of silver to be precipitated in the cells in sufficient quantity to destroy them combined with the frequency of application that makes the weak solution most potent in causing a stain.

"To recapitulate briefly then as far as argyrosis is concerned:

"1. The essential element in determining the stain is the soluble chlorides of the tissues.

"2. It is chloride of silver that is decomposed by light in an albuminous material.

"3. The soluble chlorides influence the rate of penetration of silver nitrate.

"4. The depth of penetration is a function of the concentration of the silver solution.

"5. The seat of the stain is determined by the soluble chlorides and is also dependent on the strength of the solutions.

"6. The brown stain is either argentous chloride or an oxychloride of silver.

"7. The black stain is either metallic silver or the black oxide, probably the former.

"8. Drops are more potent in causing a stain than an application of a stronger solution by the brush.

"I should like to add a word upon the organic preparations of silver.

"From my experiments which were undertaken with a view to ascertain their penetrating power as compared with solution of nitrate of silver, I must confess that my former faith in them which never was very great, has now almost ceased to exist. One cannot go into them individually here, in fact I have not tested them all yet but one can speak of argyrol and of its ally collargol which are perhaps the most disappointing specimens of the lot. The penetration of a 20 per cent solution of argyrol as compared with weak nitrate is practically nil, and one was not surprised to find this, as the molecules of these organic silver compounds must be large and if so must exert a powerful influence on the action of the body they collectively represent. Then again we know that organically combined silver is very inert as compared with the inorganic form. The amount of silver such bodies contain is no criterion of their therapeutic utility. The all-essential point is that any of the large amount of silver enters into a reaction whereby it changes its electrical state and stability from that of its initial to that of its final state. If so, then it has some potential energy behind it. Argyrol does not react with a soluble chloride and most of the silver is deposited as such on adding a dilute acid. I believe it is wholly inert in the conjunctival sac or at any rate almost so. Its intense color is a false expression of its energy. I have read of an experiment which consisted in placing a piece of catgut in a solution of argyrol and after some hours finding it had percolated through and through. The experiment was to show its intense power of penetration. Untwist a strand of catgut and note the fibers it is composed of and see how absurd it is to assume great penetrative power on the part of a liquid which finds its way between a few fibers of catgut. Argyrol may have a mechanical effect, I do not deny this, and its sedative action is due to the large amount of silver it contains (metallic silver is sedative in its action), but when this is said I believe we have summed up argyrol. It is interesting to note the comparative rarity of staining by argyrol or any other organic silver compound. (Protargol gives a reaction with a soluble chloride so I do not include it). One is gratified to see from the report of the Special Committee appointed by the British Medical Association to investigate the bactericidal action of the various silver compounds that their results are in accordance with those of the writer. Approached from an entirely different standpoint they are led to conclude that the amount of silver a compound may contain is no criterion of its bactericidal power and the same conclusion the writer would extend to properties other than bactericidal. I am quite aware, judging from the extensive literature on the therapeutic uses of the organic silver salts and the praise that has been accorded them, that my ideas rank with those who are in the minority but they are based on convictions which I trust are well grounded and one's remarks are presented with all respect to those who have labored in the same field with more favorable results.''

It is apparent in the case of generalized argyria that an ionizable compound of silver is being dealt with and that when taken internally in the presence of hydrochloric acid it is converted into the chloride. The gastric contents also contains hydrogen sulphide, amino compounds and complex protein derivatives. Purine compounds form insoluble precipitates but silver chloride and silver alone combine readily with amino compounds, and albuminates, and albumoses yielding soluble preparations which may be carried directly into the blood stream and later deposited in the various parts of the body. Likewise, the formation of colloidal silver preparations when they are introduced into the circulatory system, may easily take place. These new colloids may be easily destroyed when they reach a field where their charge is neutralized by electronic affinities of sufficient magnitude carried by body colloids. The same applies to the colloidal preparations where the electronic affinities are weakly held in place by the introduction of small quantities of protein material (colloidal Ag 70 per cent and 30 per cent protein). The physical properties of these types of drugs are determining factors in regard to the intoxication. For example, the charge of the colloidal particle, the difference of potential between particles and the medium, the radius of the particle, the distance between the Helmholtz layers, the specific inductive capacity of the liquid, the measure of the facility of slipping, the viscosity of the liquid, and the mobility of the particle are prime factors which tend toward the precipitation of the drug in the tissues as a result of coagulation. It amounts to a change from the suspensoid phase (disperse) into the coagulate condition as a result of the discharging of the colloidal particles in the presence of ionized molecules or colloids of an opposite charge illustrated by the action of mols of aluminum sulphate on colloidal silver or gold solutions. Argyrism is practically on the same basis as dyeing. Burton (1921) page 209, very aptly expresses these views as follows: "Modern accounts of the process of dyeing take into consideration the colloidal state for two reasons: (1) the textile fibers to be dyed are colloidal in their nature, and (2) many of the dye solutions are true colloidal solutions. Michaelis, Freudlich and Neumann, and Biltz and Pfenning have separated the dyes into three classes with regard to their colloidal nature: viz., (1) those in which nearly all the substance exists as visible ultramicrons and which may easily be subjected to dialysis, (2) those in which the substance exists as a mixture of submicrons, amicrons, and possibly molecules and which may be dialysed but only at a very slow rate, and (3) those which contain no visible ultramicrons but which show fluorescence and diffuse readily through parchment paper."

To conclude, the physical chemical nature of the chemical is a large factor predisposing toward the intoxication. These physical factors are just being appreciated in their relation to the therapeutic use of drugs which enter into the blood stream whose physical factors are so nicely balanced that the introduction of foreign substances out of equilibrium with the human organism often create untoward results which are not quickly adjusted by our economy.

The favorable factor to be dealt with is the protective action of certain colloidal solutions. This is such an important factor that

Zsigmondy and others have expressed the protective action of organic colloids in terms of a gold value which only means the number of milligrams of the colloid required to protect 16 c.c. of a stable gold solution containing about 0.005 per cent gold from the precipitating action of 1 c.c. of a 10 per cent sodium chloride solution (electrolyte). That this intoxication is a chemical compound readily subject to photodynamic effects is shown by the fact that KCN solution easily dissolves it from any of the sites of deposition. Metallic silver would not dissolve with ease. Danysz (1914) in speaking of his silver complexes with salvarsan writes as follows: "Orfila gave dogs 4.38 gm. of silver nitrate in pills daily for four consecutive days without observing any appreciable symptoms. Charcot (Charcot et Ball—Encyclopedie medicale de A Dechambre, vol. vii, p. 57) who at the same time as Vulvian, Cruveillier and others made numerous tests of the physiologic and therapeutic action of silver salts on man, writes on this subject (1) 'The main fact that arises from our observations on this subject is the tolerance of the economy for this medicamental agent.'

"These scholars have never observed any case of poisoning socalled, and the cases of argyria were only observed after the absorption of 30 grams of silver nitrate. They noted, on the other hand, that a prolonged treatment of this product can very favorably influence certain nervous affections which as we know today are due to infections by spirochetae."

Tweedy (1895) states that 15 grains of silver nitrate is the smallest quantity in record that has produced a generalized argyria. Riemer (1875) gives 34.032 gr. $AgNO_3$ as the amount giving the intoxication under his observation. Davidson (1916) accounts for 400 grams of metallic silver in a case of acute gonorrhea. Steiger (1917) describes a case after 4 to 6.5 grams of silver nitrate. The figures are representative of many other observations.

The time for the appearance of the intoxication varies from a few weeks to several years. The figures which are definite are found in the last column of Tables I and II.

EXPERIMENTAL

In order to investigate these points experimentally two hundred rats were injected intravenously and twenty-five rabbits were treated with repeated large doses.

(To be continued.)

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II. THE MERCURY INHALATION THERAPY OF SYPHILIS

An Historical Review

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AN interesting review of the history of mercury vapor therapy in syphilis has recently been published by Cole, Gericke and Sollmann[1] in which, however, great prominence seems to have been accorded the unfavorable side of mercurial inhalations and but little effort has apparently been made to present the favorable facts in the history of this form of treatment. It is true that the many unfortunate incidents recorded by early authors as due to mercury inhalations have served to mar the otherwise enviable record of this treatment of syphilis, but it must also be admitted that the rôle it has played in stamping out epidemics of syphilis and the good it has otherwise accomplished have not only completely overshadowed the defects ascribed to it, but have even earned for it great eminence as a therapeutic procedure.

Mercurial inhalation therapy enjoyed great popularity in the past. During the Middle Ages, when syphilis was epidemic throughout nearly all of Europe, necessitating the closing of all social establishments and of public baths, in the effort to check contagion and its ravages, mercury inhalation was practically the exclusive weapon with which the plague was fought, and was the only means in the hands of almost all the prominent physicians of that time to combat the disease. There is much literary evidence on record testifying to the immense use formerly made of this method of administering mercury, and this in spite of the fact that many unfavorable factors were associated with it; the good it accomplished evidently justified the disregard of untoward by-effects. Its beneficent results at that time constitute an honorable chapter in the history of mercury therapy.

Mercury inhalation, like every therapeutic procedure, every theory, dogma and discovery in medicine, has had its friends and foes, its staunch supporters and its adverse critics, its periods of glory and of villification. But on the whole, medical literature is not unfavorable to this form of treatment; on the contrary, its record compares favorably with that of other long-time medical measures.

Mercury has been in use since a very early period of drug therapy[2] and is said to have been used by the Chinese in ancient times as a remedy for syphilis. It is also thought to have been employed for this purpose in India, in Egypt and in Greece. In Greece it was primarily a remedy for skin diseases and later, when syphilis appeared, its application to this disease, because of its skin manifestations, was a natural sequence. Hieronymus Fracastorius,[3] 1530, was a staunch supporter of mercury vapor therapy. In his treatise on syphilis, he first advises the use of caustic for the initial lesion and then continues by saying—"But it is in vain, I suppose, that you have exhausted the entire series of these remedies; or, perhaps, impatient of such slowness, relying upon your strength and your health, you resolve to turn to more energetic agents to end the matter with the hated enemy as soon as possible. Be it so! I will show you this violent and expeditious method which can triumph in a short time over a disease that is usually long in duration, stubborn, subject to relapses and rebellious to mild medication. First of all, here is a treatment which consists in the use of fumigation composed of styrax, of cinnabar, of minium, of antimony and of incense. We have here without doubt an active medication which succeeds in cleaning the body of its awful taint."

Astruc[4] 1736, relates that when syphilis became epidemic in Europe, mercury vaporization was so extensively used, that almost all European physicians of any note availed themselves of this method of treating the disease. He mentions, among others, Massa, Bolognino, Fallopius, Mattiole, Rondelet and Cataneus. He, too, calls attention to the fact that the application of mercury to syphilis came about by a process of analogy, inasmuch as the European physicians were already familiar with its use in leprosy, scabies, smallpox and other diseases with dermal symptoms. In his time mercury was applied externally in four forms—ointments, plasters, washes and "perfumes." "Perfumes" consisted of some form of mercury mixed with other substances, such as aromatic oils, and they were administered by vaporizing these mixtures in one way or another; but inhalations were used most extensively and in preference to all other methods.

Fournier[5] contributes a very interesting chapter to the history of mercury inhalation. He writes: "The treatment of syphilis by mercurial fumigation is nearly as old as the inunction treatment. Having been successfully used in cases of chronic scabies, it was also applied to the skin eruptions of the 'new disease.' Fumigations were in great favor in former times and, as they were then performed, constituted an excellent means of accomplishing the 'good salivations' which were then considered necessary to eliminate the corrupt humors.

"The *old* treatment, which was called the treatment by 'perfumes,' consisted in preparation, fumigation and sudation. The preparation, as in the case of inunction, included bleeding, purging and the use of so-called alterative and depurative remedies. After this the patient, quite naked, was put into a kind of small tent, or in a closed and heated chamber. Near the patient was placed a brazier in which tablets were thrown to produce fumigation. These tablets were of complex composition and besides containing various mercurial preparations, such as cinnabar, calomel, red precipitate, turpeth, etc., also included substances intended to cause a dense smoke, such as fats, resins, incense, mastic, oliban, benzoin, aloes, styrax, etc. The patient was exposed to this hot and smoky vapor for half an hour or more, according to his strength. It is needless to say that he emerged in a half suffocated condition. However, if he showed signs of swooning, he was allowed to breathe pure air by means of a tube passed into the tent. Finally, the patient was put into a hot bed and covered with bedclothes and left to perspire for an hour or two. This procedure was repeated every day, or every other day, according to the strength and power of resistance of the patient, for it was no light affair to endure such semi-asphyxiation.

"The accidents that might result from such a brutal practice are easy to imagine; for it was not only fumigation of the skin, but also mercurial inhalation, the patient having his head plunged by the half hour in mercurial vapors which penetrated the lungs and the organism in indeterminate doses. In fact, this practice was prolific of disasters, which are admitted by the old authors with naive resignation. First of all, it produced what was desired, namely, profuse salivation, which according to Fallopius, lasted seven or eight days, during which time the patient spat out from six to eight pounds of saliva. Besides this, it caused a series of accidents, some immediate and others sequential—such as suffocation, asthma, bronchitis, pulmonary catarrh, ophthalmia, headache, diarrhea and sometimes graver symptoms which the author describes as debility, cachexia, marasmus, convulsions, epilepsy, apoplexy, paralysis, etc. Sometimes things went even further, and fatal cases are reported by Fallopius and others."

It is not at all difficult to comprehend that such "mercury applications" as Fournier describes were attended by "violence, irritability and uncertainty;" the respiratory and other symptoms they caused must have sometimes been extreme. Cinnabar, calomel, red precipitate, turpeth, and other mercurial combinations are objectionable in themselves because of the fumes they emit when heated; while the resins and oils when volatilized are irritating to the respiratory tract, and this, of course, would not improve the treatment. Minium produces lead poisoning symptoms, another undesirable feature. Such crude methods of giving mercury inhalations as were in vogue in olden times, and not the mercury inhalations proper, were undoubtedly the cause of the many complications described. Even in an era when the subjects are reputed to have been of stronger physique than our present-day patients, such methods of applying mercury must often have been quite unendurable.

Nevertheless, in spite of the accompanying complications, the benefits of mercurial inhalations and fumigations were so decidedly manifest, that this method of treating syphilis was predominant. Still, efforts were made to eliminate its dangerous and unpleasant complications, due to admixtures, to impure and improper mercurials as well as to faulty administration. Those complications were to some extent eliminated later by other and better methods of generating and administering the mercury vapors. "Nowadays," Fournier adds, "the method is not modified but transformed, and no one is now killed by fumigation. * * * * After this the burlesque practice of what was called 'preparation' was abandoned. Salivation was then given up and was generally regarded not as a beneficial result, but as a complication of the treatment. Finally, the famous 'perfumes,' which only served to suffocate the patient, were also banished.

"On the other hand, the most inoffensive preparations of mercury were sought. Formerly cinnabar, gray oxide and impure calomel were used; but cinnabar is liable by heat to decomposition and to the production of sulphurous acid, which is very irritating; the gray oxide gives rise to dioxide, which is too energetic; dry calomel gives off hydrochloric acid, although this is not produced when it is volatilized in contact with steam. So that after many experiments we now use only very pure calomel and only volatilize it in the presence of steam. Fumigation as it is now practiced is a very simple affair * * * *".

Lalouette[6] regarded fumigation as superior to all other means of administering mercury and proved his contentions in a number of cases treated by him in the presence and under the supervision of eminent physicians, surgeons and officials, who attested to the cure of the patients so treated. He devised a cabinet for mercurial fumigation which was essentially like those used at present; he also prepared special powders for use in particular syphilitic conditions. He played a very active part in reviving the mercury vapor system of therapy which was then in ill repute because of the unfortunate accidents that had often resulted from it.

Jackson[7] of Northumberland, used calomel vapors very extensively. He generated these in a very convenient apparatus devised by him. S. Solis Cohen[8] in his discussion of inhalations, informs us that in India and Arabia the inhalation of mercurial vapors has been practiced for ages for the purpose of exciting salivation in the treatment of certain diseases. He further states that "the inhalations of vapor from cinnabar were employed at a very early date in the treatment of constitutional syphilis." The method employed there is as follows: The patient is covered with a blanket beneath which is burned a candle composed of cotton cloth, smeared with melted beeswax and impregnated with an equal quantity of cinnabar, the smoke therefrom being inhaled into the respiratory tract.

In our day mercury inhalation therapy is still the predominating method of treating syphilis in those countries where smoking is indulged in by all, young and old, male and female. In Turkey, Arabia, Persia, India and African countries, mercurial inhalation still constitutes a common method of administering this drug. The Persians, according to Polak[9] seldom apply to the resident European physicians who treat syphilis by modern methods, but seek rather the assistance of native quacks of either sex. These have their special formulas, but the ordinary prescription is inhalation from pipes containing tobacco mixed with cinnabar. These pipes are smoked once or twice daily; the smoke is inhaled, held for some time in the nose and mouth, and exhaled. Sometimes a pill containing arsenic is added to the inhalation treatment. Polak finds that in Persia, although acquired syphilis is frequent, congenital syphilis is comparatively rare. This he attributes to the permanent cure of the disease in the parents, which is accomplished through their use of mercurial inhalations, and which eventuates in freedom from infection in the offspring. If the absence of congenital syphilis is a fact, and Polak's explanation correct, it is a matter of transcendent importance which ought to render this method of treating syphilis a problem of the greatest consequence.

The literary evidence setting forth the extensive and beneficial use of mercury vapor is much too exhaustive to treat in detail. Every one familiar with its history will affirm that this method of combating syphilis was looked upon in the past with great favor and that the good service it rendered humanity is indisputable. In confirmation of the high reputation this treatment has enjoyed and the great esteem in which it was held, the words of Fournier may be quoted: "But if we examine the facts, we find a series of observations proving that fumigations have cured syphilis of different kinds more or less rapidly. Such, for example, are the cases reported by Harteloupe concerning the different forms of secondary syphilis, such as vegetating mucous patches, ecthyma, etc., on which this mode of treatment exerted a beneficial action.

"It is undeniable that mercurial fumigations favor the cure of certain specific dermatoses, especially those of an ulcerative nature." He also suggests the use of mercurial flannels, regarding the absorption of mercury vapor from these as a fundamental treatment of syphilis. By this means it would be possible to avoid certain defects of ordinary inhalation, namely, stomatitis, bronchial catarrh, laryngeal spasm and debility caused by the profuse, repeated sweatings, etc.

Lalouette recommends inhalation because it combines safety with convenience and he affirms that twenty to twenty-five fumigations were sufficient to cure his ordinary cases of syphilis. He also quotes

Langstone, Parker, Henry Lee, Bumstead, Duncan, Wilders and Harteloupe who lauded its curative properties. Zeissl[10] and others treated their syphilitic patients for many years by mercurial fumigation in the Vienna General Hospital after the method prescribed by Henry Lee of London.

There are on record many such instances showing that clinicians of all countries and continents have utilized mercurial inhalations in the treatment of their syphilitic cases and have praised the method.

An unbiased and open-minded examination of the literature shows that looked at from the historical standpoint, the treatment of syphilis by mercury inhalations is not to be dismissed as either obsolete or unimportant. On the contrary, if the achievement be judged from its recorded history, it may be claimed without hesitation that this method has a far more reputable status than Cole, Gericke and Sollman seem inclined to accord it.

CONCLUSIONS FROM HISTORY

1. That mercury vapor inhalation therapy has been employed very extensively in many countries and for many centuries.
2. That numerous competent physicians in almost all countries and almost all times utilized this therapeutic factor in the cure of syphilis and other diseases.
3. That whenever mercurial vapors were administered in sufficient quantities they never lacked action, having produced always some definite effect, either desirable or undesirable.
4. That pure metallic mercury was rarely used, but the drug was commonly employed either impure or in chemical combination.
5. That complications occurred most frequently when other substances were added to the mercurial compounds.
6. That the older physicians for one reason or another mixed the mercurial substance with foreign, mostly undesirable ingredients.
7. That the vaporization process of mercury mixtures was conducted in a multitude of ways, and the vapor administered in an indiscriminate manner.
8. That all early methods of generating and administering the vapors were, to say the least, crude, unscientific, if not ridiculous.
9. That the preponderance of evidence is in favor of claims for the beneficent properties of inhaled mercury vapor.

10. That while there is much in the past history of mercury vapor therapy that is unfavorable, there is much more which commends the method and places it among other well recognized and lauded therapeutic procedures in the history of medicine.

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A CASE OF SYPHILITIC RE-INFECTION

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THIS case is of interest because of the short interval between the first and second infection, and the rapid response to therapy in each instance.

Modern medical opinion is converging more and more to the belief that syphilis does not produce immunity and that re-infections are not only possible but do occur. At least medical literature records sufficient evidence to support this view. White[1] in a study of twenty-eight cases of syphilitic re-infection maintains, firstly, "that a re-infection can take place and secondly, that such re-infection cannot take place until the original infection has been completely cured." Jacob,[2] Williams,[3] Benario,[4] Lesser,[5] Minassian,[6] Brenn,[7] Panton,[8] and others have likewise reported authentic cases of syphilitic re-infection. In most all of these reported cases the second infection developed over two years after the first attack except in the case reported by Panton where the interval was eleven months. In his case the initial lesion of the first attack was genital. In the second infection, the chancre was extragenital, being situated on the lower lip.

Besides the clinical, serological and bacteriological evidence an added proof in the recognition of a re-infection is the history of recent exposure, in fact, a thorough study of the case is essential in order to satisfactorily determine that an earlier attack had been entirely eliminated and a fresh infection set in.

The case herewith reported, male, age twenty-six, first came under observation on September 27, 1920, presenting a slowly disappearing primary lesion on the glans penis. There was a distinctly palpable bilateral inguinal adenitis, a fairly marked secondary macular and papular syphilide covering the entire body and a painful, ulcerating mucous patch in the anus. The time that had elapsed since the appearance of the initial lesion was about seven weeks. The duration of the mucous patch was ten days. Wassermann test showed a four-plus reaction.

The therapy consisted of five arsphenamine injections in doses of 0.6 given at intervals of from three to five days, depending upon toleration. The lesions cleared up with unusual rapidity, completely disappearing within thirty days after the initial arsphenamine injection. The patient returned on December 20, 1920, at which time a Wassermann test was made which showed a negative reaction. There were no further clinical manifestations.

On February 12, 1921, approximately two months after his last Wassermann test, the patient returned presenting a small, typical ulcus durum on the penis. There was a history of recent exposure. The duration of this lesion was about six days. There was no perceptible swelling of the inguinal lymphatics or other manifestations present. Dark-field examination showed numerous, highly motile treponemae. The Wassermann test was negative.

The therapy consisted of three neoarsphenamine injections in doses of 0.9 given at intervals of from three to five days, depending upon toleration. The lesion disappeared completely within ten days. The patient had to leave town and returned the following month. A Wassermann test made showed a negative reaction. Repeated Wassermanns have been made from time to time since then, all showing negative results.

The outstanding points of interest in this case are: that this patient developed, and it is reasonable to believe was completely cured, of two separate and distinct syphilitic infections within a period of less than ten months; furthermore, that the clinical and serological response was unusually favorable under a rather mild antiluetic medication. The duration of the first infection was approximately three months; thence an interval of less than two months, followed by a second attack of probably one month.

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THE WASSERMANN REACTION IN PREGNANCY*

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THIS is a study of the Wassermann reaction on the blood of 10,427 pregnant women. The tests were made during the period from June, 1915, to June, 1919, and formed a part of the routine examination of these women. The paper is presented to draw attention to the efficacy of cholesterinized antigens in the Wassermann reaction in pregnancy and also to give some idea of the prevalence of syphilis among women of the dispensary class.

The method employed[1] utilizes two cholesterinized antigens prepared from a plain alcoholic extract of human heart muscle and a more sensitive antigen, also cholesterinized, made from guinea pig hearts. Sheep's cells are used as the indicator substance.

The test is so adjusted that a positive reaction is reported when there is complete inhibition of hemolysis with all three antigens, or partial inhibition with the least sensitive antigen, and no hemolysis with the other two. A *doubtful reaction* shows partial or complete inhibition with the two more sensitive antigens and complete hemolysis with the weakest. A negative reaction shows complete hemolysis with all antigens. The weakest antigen rarely gives any degree of positivity when the other antigens show a negative reaction.

The results obtained in this study should be compared with the following which we obtained by the same technic in a group of 3701 naval students, and in a penal group of 864 women:

	TOTAL	POSITIVE		DOUBTFUL		NEGATIVE	
		NO.	%	NO.	%	NO.	%
U. S. Naval Aviation Students	3701	21	.56	19	.51	3661	98.92
Inmates of Mass. Reform. for Women	862	349	40.49	75	8.7	438	50.81

The purpose of citing the above figures, which are from a highly syphilitic and an essentially nonsyphilitic aggregate is to point out the comparative prevalence of the disease in well defined groups when determined by the Wassermann test when it is performed with the same uniform technic. Even a minute description of the method of testing does not necessarily give an idea of its efficacy, because variations in its execution by different workers may result in discrepancies in the results while essentially different methods may give rise to none. This fact was demonstrated by a recent comparison of the reactions obtained in six different laboratories. The same specimens were tested by the same method and reagents—antigen, amboceptor and cells. The rate of diluting the antigen was not constant, although all other factors were the same, and yet distinct variations were shown in the final readings.

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In the present study, the specimens of blood were obtained from each patient as admitted to the following institutions: Boston Lying-In Hospital, the Lowell Corporation Hospital, the Florence Crittenton Home, and the New England Hospital for Women and Children. At the Boston Lying-In Hospital the specimens were usually collected during the first five months of pregnancy. At the Lowell Corporation, they were obtained a few days before delivery or very soon after. At the Florence Crittenton Home, they were secured before admission for confinement. The last institution admits only unmarried primiparae. The specimens from the New England Hospital were secured by expressing blood from the placental end of the umbilical cord after delivery and for this reason its results will be treated separately.

Table I shows the figures for the entire group:

TABLE I

WASSERMANN RESULTS IN 10,427 CASES OF PREGNANCY

	TOTAL	POSITIVE		DOUBTFUL		NEGATIVE	
		NO.	%	NO.	%	NO.	%
Boston Lying-In Hospital	7121	372	5.24	353	4.95	6396	89.7
Flor. Crittenton Home	264	11	5.6	16	5.97	237	88.6
Lowell Corp. Hospital	370	9	2.43	5	1.33	356	96.2
N. E. Hospital	2672	41	1.57	31	1.12	2600	97.5
Totals	10427	433	4.18	405	3.85	9589	91.9

The percentages of the positive and doubtful reactions in the first two institutions are quite different from those in the last two. The results for the New England Hospital can be explained easily by the manner of obtaining the specimens, and they agree with the observation of others, that "cord blood" is only about one-third as effective in the detection of syphilis by the Wassermann test as that obtained by the usual venous puncture. The table also indicates a low incidence of positive reactions in the cases from the Lowell Corporation which, as will be shown later, is accounted for by the fact that roughly 80 per cent of the individuals are of foreign birth or descent. The figures from the Florence Crittenton Home are particularly interesting inasmuch as only young unmarried women without evidence of gonorrhea or syphilis are admitted for confinement. These, therefore, should represent unsuspected cases of syphilis.

TABLE II

WASSERMANN REACTION BY RACE-GROUPS

	TOTAL	POS.	PER CENT	DOUBT.	PER CENT	NEG.	PER CENT
American	1665	107	6.42	78	4.68	1480	88.9
*Russian	1566	44	2.81	56	3.58	1466	93.7
Jewish	561	14	2.49	27	4.71	520	92.6
Italian	868	33	3.8	41	4.72	794	91.4
Irish	501	19	3.79	20	3.99	462	92.9
*Polish	313	7	2.25	10	3.22	296	95.
Austrian	274	9	3.28	7	2.55	258	94.2
Syrian	191	12	6.28	12	6.28	167	87.3
Negro	276	92	33.3	7	2.54	177	64.1
Greek	330	3	.91	7	2.12	320	96.8
Canadian	193	11	5.7	7	3.62	175	90.7
English	113	6	5.3	2	1.77	105	93.
French	91	—	—	3	3.28	88	96.6
Portuguese	65	4	6.16	4	6.16	57	87.7
German	54	—	—	2	3.7	52	96.3
Swedish	46	1	2.175	1	2.175	44	95.7
Scotch	34	3	8.83	2	5.89	29	85.3
**Miscellaneous	153	14	9.14	8	5.23	131	85.3
	7294	379		294		6621	

*These are almost all Russian or Polish Jews.

**Consisting of Finns, Turks, Nova Scotians, Danes, Swiss, Lithuanians, Norwegians, Roumanians, Hungarians, Prince Edward Islanders, W. Indians, Porto Ricans, Newfoundlanders, Dutch, Servians, Bulgarians, Chinese, Belgians, Asians, Albanians, Spanish, Japanese, Cape de Verde Islanders, Algerians, Cubans, Galesians, Persians, Egyptians.

Information of the greatest value was obtained by dividing the patients into racial groups. The classification used is based on the nativity of parents except where racial distinctions are universally recognized, as illustrated by the Jews, Chinese, Japanese, and Negroes. This classification is employed by the U. S. Bureau of Statistics in separating immigrants.

Besides indicating the percentage of positive reactions in the racial groups studied, Table II also serves to check the efficacy of properly standardized cholesterinized antigens during pregnancy. Among 330 Greek women only 3 or 0.9 per cent gave a positive reaction. If we assume, for the sake of argument, that these three positives are nonsyphilitic, the percentage of false positive reactions obtained in the entire group could not exceed 0.9 per cent. On the other hand, the extreme delicacy of cholesterinized antigens is borne out by high incidence of positive reactions among negroes—33 per cent.

The incidence of the doubtful reactions varies but slightly in the larger groups (from 3.6 to 4.7 per cent) and is usually nearly equal to the positives for a given race. A notable exception occurred among the negroes where the percentage of doubtful reactions was only 2.5 as compared with the 33.3 of positive tests. If our experience is correct that about half of the doubtful reactions represent treated cases of syphilis, these figures would indicate that the infected colored group has not received adequate antisyphilitic treatment or when treated readily respond as determined by serology.

Although the number of cases in some of the groups is relatively small, it is evident that there is a lower rate of positive reactions among the foreign population. The one exception lies with the Syrians who show about the same percentage as the whites born in the United States and Canada.

Attention is also drawn to the fact that the positive reactions bore a strict relation to races regardless of hospitals. A separate analysis of 200 Americans and 64 Canadians from the Lowell Corporation Hospital and the Florence Crittenton Home showed 6.7 per cent positive reaction, figures very similar to 6.42 per cent and 5.7 per cent shown by the entire group of Americans and Canadians in Table II. The Greek group was unusually low in both the 178 cases from the Lowell Corporation Hospital, and the 192 from the Boston Lying-In Hospital.

An analysis by age groups is given in Table III.

The noteworthy fact to be learned from this table is that congenital syphilis must play a very small part in maternity. If we

TABLE III

WASSERMANN RESULTS CLASSIFIED ACCORDING TO AGE-GROUPS

AGES	TOTAL	POS.	PER CENT	DOUBT.	PER CENT	NEG.	PER CENT
12-17	110	1	.91	5	4.54	104	94.6
17-22	1262	72	5.21	71	5.13	1119	88.7
22-27	2889	130	4.50	78	2.70	2681	93.8
27-32	1505	65	4.34	71	4.73	1369	90.7
32-37	981	46	4.65	31	3.17	904	92.2
37-42	482	19	3.94	11	2.28	452	94.8
Over 41	163	3	1.83			160	97.5
	7392	336		267		6789	

assume the single positive case among the 110 ranging from 12 to 17 years was congenital syphilitic, the incidence is less than 1 per cent. This is greatly below that of the five groups over 17 which constitute the majority of cases.

Since pregnancy is a natural physiologic function, few if any of these women sought medical attention because of acute or chronic illness. We have found that individuals of greater intelligence have shown uniformly a lower incidence of positivity, while those of the lesser mentality a larger rate. This difference is shown by comparing the 3701 Naval Aviation students who showed only 0.5 per cent positive reactions, with the group of criminal women who are for the most part feeble-minded, with a positive rate of 40.1 per cent.

Therefore, we conclude:

1. That the statistics in this paper should indicate the prevalence of syphilis among the average women of Massachusetts of the dispensary class.

2. That if we consider a positive reaction as diagnostic of syphilis, as in 4.18 per cent of these cases, and a doubtful one as indicative of inadequately treated syphilis, as in 3.85 per cent, the total incidence of the disease in this class is 8.03 per cent.

3. That in our experience, properly standardized cholesterinized antigens have yielded a negligible number of false positive reactions in child-bearing women.

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REACTIONS FOLLOWING ARSENOBENZENE ADMINISTRATION AND THEIR TREATMENT

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IT HAS been observed by Ehrlich and others that in certain instances the administration of arsenobenzene is followed by untoward symptoms which may at times be very severe and even end fatally. Wechselmann and others doubted the toxicity of salvarsan and gave various explanations for these disturbances. Some claimed faulty technic; some flooding the tissues with proteins derived from the destroyed parasites, and others a constitutional weakness of the lymphatic and vascular systems.

It has been calculated that the chances of death are as follows (Meirowsky).[1]

Following	salvarsan.	1 in 13,000
"	sodium salvarsan.	1 in 20,000
"	neosalvarsan.	1 in 162,000

Reactions following arsenobenzene may be classified as:

(1) Early Effects:
  (a) Those occurring during the injection.
  (b) Those occurring within 24 hours of the injection.
(2) Late toxic effects.

(1) EARLY EFFECTS

(a) Those occurring during the injection.

1. *Vasomotor Symptoms.*—These occur only during intravenous injection and constitute the so-called "anaphylactoid" or "nitritoid" crises. These are normally slight but may be unusually severe. The usual symptoms are flushing, swelling of the lips and

tongue, puffing of the face, dilation of the pupils, rapid pulse, cyanosis, dyspnea and occasionally, precordial pain or distress accompanied by cries of agonized fear. In more severe cases there is great respiratory embarrassment and on two occasions we have seen respiration cease entirely. As a rule recovery is very rapid but occasionally symptoms persist for several hours. Hyman[2] has suggested that this type of reaction occurs in patients of the so-called "plethoric disposition" but the writers have observed perfectly normal individuals react violently. Fortunately such alarming cases are few.

2. *Syncope.*—It is fairly common for a patient to faint during or immediately after an injection. This occurs usually after only the first dose, but may occur at other times and then is frequently due to taking a meal a short time before receiving the injection. In the latter case the patient is violently sick and has subsequent severe headache with a rise of temperature.

3. *Pain in the Gums and Teeth.*—This is a transient condition and is probably due to vasomotor changes, the added congestion in the gums producing the pain. It should be noted that arsenobenzene aggravates an existing mercurial stomatitis.

4. *Peculiar Taste in the Mouth.*—This is a sign of no importance but in some cases appears immediately the first few drops have entered the vein. We have known patients who were able to tell the operator accurately when the vein was successfully entered by the prompt occurrence of this phenomenon. The taste usually is described as a metallic one, and occasionally is accompanied by a sense of sweet smell. At other times it is described as resembling garlic, vinegar, chloroform, or paraffin.

(b) *Those occurring within twenty-four hours of the injection*:

1. *Rigor, Headache, and Rise of Temperature.*—Within limits these have been described as normal sequelæ to the intravenous administration of arsenobenzene. When they reach proportions calculated to upset the patient they must come within the group of reactions. These symptoms go to form by far the most common type of reaction. They come on usually within two hours, as a rule after only the first injection, and have passed off by the following day.

2. *Vomiting and Diarrhea.*—These are usually very slight and in fact are rarely seen. Occasionally they are severe and are accompanied by pains in the abdomen, back, bones and joints, and cramp

in the legs. On these occasions the urine is scanty, distinctly alkaline and shows traces of albumin and a few casts. Again they usually follow the first dose only.

3. *Herpes Labialis.*—Severe herpes is rare; a mild herpes of the lips is exceedingly common but seldom looked for. As a rule it follows the first injection and does not reappear. It causes so little trouble that the patient seldom brings it to notice. In some cases a labial herpes follows every dose. One remembers a Colonel, who was being treated privately, complaining that his officers could tell exactly when he had had treatment by the occurrence of a severe labial herpes which had developed fully by dinner time on the same day. Herpes of the buccal surfaces, pharynx and larynx also occur.

4. *Skin Eruptions.*—These may be urticarial (which is not uncommon) macular, papular, follicular, polymorphic, or erythematous. These however are usually transient.

5. *Edema* which may be general or localized to the face and hands. When this toxemic manifestation lasts more than a few hours it is accompanied by an erythema. Edema of the optic discs is a well recognized phenomenon occurring during the course of a dermatitis.

6. *Coryza* which is severe but transient.

7. *Hepatic Tenderness* which is usually limited to the region of the gall bladder.

8. *Injection of the Conjunctivæ.*—This symptom may occur alone or with erythema, edema, or coryza.

9. *Hypersalivation* is an infrequent occurrence. It may be mercurial in origin and aggravated by arsenobenzene.

10. *Aggravation* of nonluetic conditions has been noted by W. H. Guy of Pittsburg.[3] In these cases a few bronchial râles would develop into a mild bronchitis or bronchopneumonia and many other pathologic conditions tended to exhibit aggravation. Tuberculosis patients, however, showed no unfavorable reaction.

Causes for These Reactions.—A multitude of explanations for the occurrence of these reactions has been offered from time to time. In the early days of salvarsan they occurred much more frequently than at the present time and one must conclude that errors in technic played an important part in deciding their incidence. The toxicity of the drug was also a factor of possible importance.

This is now practically eliminated by the strict biologic control of all issues of the various preparations. A third factor undoubtedly is the susceptibility of the patient. This usually is estimated after the first dose but may not appear until many doses have been given.

Wechselmann considered that the liberations of endotoxins from dead parasites was the chief cause. This explanation, however, is no longer tenable, for similar reactions have followed in patients not infected with any organism on which arsenobenzene is known to act.

McIntosh and Fildes have blamed the protein derivatives of dead bacteria which were present in the water before sterilization. This can be avoided by sterilizing the water immediately after distillation and using it immediately the flask is opened.

Too concentrated solutions of arsenobenzene and imperfectly dissolved neoarsenobenzene must share to a certain extent in the responsibility.

As already indicated, failure to prepare the patient beforehand is responsible for many early reactions. The presence of partially digested food in the gastrointestinal tract and the imperfect cleansing of the alimentary canal as a whole are determining factors in many febrile and gastrointestinal disturbances.

Case 1.—The patient, a robust male of nineteen, was suffering from a primary lesion in his coronal sulcus. Spironema pallidum was demonstrated and his serum Wassermann reaction was negative. After the routine preparation which included two ounces of magnesium sulphate the night before, no breakfast on the morning of administration, and the examination of his urine which was found albumin-free, he was given 0.3 gm. of galyl. On completion of the intravenous injection the patient got down off the table and, without warning, collapsed on the floor. He gave a kind of gurgling cough, there was great swelling of the vessels of the neck and he became instantly cyanosed. Within a minute breathing stopped completely and the wrist was pulseless. Artificial respiration was commenced immediately and within about a minute and a half respiration restarted. The cyanosis disappeared very quickly, the pulse recovered and the patient was put to bed. He recovered completely within an hour. Three more doses were given at seven-day intervals without bad effect. Before the fourth dose (i.e., the sixth dose of the series), however, he again consumed a meal surreptitiously. After 0.3 gm. of galyl intravenously, a similar reaction followed while he was still on the table. Recovery was more rapid on this occasion but the immediate picture was in every respect similar to that of his first reaction. Thereafter during the breakfast hour he was locked in a side room on the mornings when he was due for treatment and his intensive course was completed without any further alarming incident.

The susceptibility of the patient varies a great deal. It is impossible to tell by examination of an apparently normal patient whether he will tolerate the drug or not. Hence the need of caution and close observation during the early doses. This point is rightly emphasized by Martin[4].

Attention to the signs of intolerance very often will enable one to avoid an attack. Alcoholics are generally more susceptible and this probably is due to the already diseased condition of the renal vessels and the vessels generally. It is interesting to note that Stokes and Busman[5] have investigated a toxic agent in a certain brand of gum rubber tubing which, when new, was responsible for serious reactions following intravenous arsenobenzene administration by the gravitation method. An interesting case of extraordinarily marked idiosyncrasy was recorded in the Practitioner.[6] The patient was sent to hospital with a secondary rash as a case of measles. There syphilis was diagnosed and salvarsan was given. The first dose (0.30 gm.) was followed by severe dermatitis. When he recovered from this he was given 2.50 c.c. intramine intramuscularly before arsenical treatment was attempted. A papulovesicular eruption, later vesico-bullous in character, appeared after the intramine injection but there were no other symptoms accompanying the rash which disappeared in 3 weeks. It was most persistent on the palms of the hands. Three weeks later he was given 0.15 gm. novarsenobillon intravenously and exfoliative dermatitis followed. On recovery he was discharged from the hospital with a recommendation for prolonged mercurial treatment and his subsequent history is unknown.

PROPHYLAXIS.—This may be summed up under the following headings:

1. Routine examination of the urine in every case.

2. Restriction of diet on the day of intravenous injection and cleansing of the intestinal tract with a purge given the night before.

3. Rest in bed after the injection till next morning. Careful protection from chilling of the patient is a point of importance. The vasomotor system in general should be guarded against any strain on its powers.

4. Strict attention to technic. Every ampoule should be submerged in alcohol to detect any crack which would permit of oxida-

tion of the drug. All apparatus should be rigidly sterilized and every aseptic and antiseptic precaution carried out.

5. Attention to the preparation of distilled water employed. If large volumes are injected, e.g., 10 c.c. or more, the preparation of the distilled water is important. The water from an ordinary still is collected in hard glass sterile flasks; these are plugged with wool and autoclaved. Thereafter the flasks are covered with paper dust caps and sealed. Water prepared in this way will keep indefinitely but a flask once opened must be used immediately (Fildes and Parnell).[7] When small volumes are injected, e.g., 1 c.c. these precautions with regard to water are unnecessary.

6. Attention to danger signals—which are well defined and include the following: Loss of appetite. Headache. Insomnia. Restlessness. Stomatitis. Diarrhea. Erythema. Loss of Weight. Renal symptoms. Jaundice. Sudden malaise and weakness. Cardiac weakness and irregularity. Should any of these signs appear either treatment should be suspended or the dose greatly reduced and the interval between doses prolonged. Two consecutive toxic reactions are a contraindication to further immediate arsenobenzene (Parnell).[8]

7. Stokes has suggested a preliminary hypodermic injection of atropine gr. $\frac{1}{50}$ before each intravenous administration of arsenobenzene. This appears to be a prophylactic measure of some value.

8. Appreciation of contraindications, absolute and relative. Addison's disease, advanced age, nervous lesions, advanced degenerations, uncompensated heart lesions and extreme cachexias are absolute contraindications. Relative contraindications are chronic nephritis, hypersusceptibility to arsenic, early cardiovascular changes, hemophilia, hepatic disease, alcoholism, lymphatism and, according to Costello,[9] tuberculosis. The latter, however, except where cachexia is very advanced, is seldom a contraindication.

TREATMENT.—For vasomotor disturbances the intramuscular injection of 1 to $1\frac{1}{2}$ c.c. of adrenalin hydrochloride, 1 in 1000 is regarded as specific (Milian). Purgation and diaphoresis should be employed also. Before the next injection, which should be given after a prolonged interval, the adrenalin administration is repeated. The dose of arsenobenzene should be reduced. Should a second toxic upset occur in spite of these precautions, arsenical treatment should be suspended for a month.

Pain in the gums and teeth is controlled by reducing the intake of mercury. Sometimes it is necessary to reduce the dose of arsenobenzene. Careful attention to hygiene of the mouth is important. With one type of patient this is a matter of considerable difficulty and only by a vast amount of trouble and personal attention on the part of the medical officer can the desired result be obtained.

Febrile reaction and gastric upset are treated best by rest and warmth. The diet should be closely controlled for the next day or two. The headache following the initial dose may be treated with aspirin but as a rule requires no treatment whatever.

In herpes labialis, should it prove troublesome, the best results are obtained with Lassar's paste.

(2) LATE TOXIC EFFECTS

1. *Stomatitis.*—Although probably due in a great measure to the mercury, there is little doubt that this condition is aggravated by the administration of arsenic. This is due doubtless to the increased local irritation produced. It is acknowledged that patients on combined mercurial and arsenical treatment are more liable to suffer from severe stomatitis than those on mercurial treatment alone.

2. *Pathologic Urinary Constituents.*—Traces of bile and albumen are relatively common. They should be looked upon as danger signals and procedure with dosage marked with the utmost caution. Should these signs indicate syphilitic renal mischief they will clear up as treatment proceeds. It is therefore quite common to find an albuminuria, present before treatment, disappear permanently after the first dose of arsenobenzene. Traces of sugar in the urine are more frequent than is generally supposed and should always be looked for. Bile and blood cells also are found occasionally.

3. *Suppression of Urine.*—This symptom may appear towards the end of a course of treatment and may be regarded as due to a cumulative action of the drug. Its direct action on the renal vessels is then given full play. Fortunately this condition is rare, but any diminution in the amount of urine excreted should be looked upon as a warning sign.

4. *Malaise.*—A general feeling of malaise may occur late in the course of arsenical treatment and should be considered a sign of intolerance. It may be accompanied by headache, insomnia, loss of

appetite, loss of weight, nausea, and possibly diarrhea and gastric upset. In severe cases hematemesis is not uncommon.

5. *Neurorecurrences.*—This group includes a number of nervous phenomena which occur during treatment with arsenobenzene. The cause is not clear and much controversy has resulted. The view that they are evidences of arsenical intoxication is difficult to substantiate. It seems that they are much more likely a group of symptoms representing clinical relapses of meningeal syphilis resulting from insufficient or injudicious treatment.

The symptoms of this group can be divided into two classes:

(a) Those appearing within twenty-four hours of a dose of arsenobenzene and (b) those appearing several weeks after the administration of the last dose.

(a) *Early Neurorecurrences.*—These include affections of one or more of the cranial nerves, which appear within twenty-four to thirty-six hours of an injection. Most frequently the third, sixth and eighth cranial nerves are involved. The Jarisch-Herxheimer reaction has been called in as a possible explanation. It is fact, however, that these symptoms clear up with further active treatment.

(b) *Late Neurorecurrences.*—This is the more important group. It includes affections of the cranial and, less frequently, the spinal nerves. The oculomotor and auditory nerves suffer most. Such symptoms as paresis of certain eye-muscles, inequality of the pupils, vertigo, labarinthine deafness, sluggish reflexes and cardiovascular changes occur. Implication of the facial and trigeminal nerves is less common. Optic atrophy, the occurrence of which sealed the doom of atoxyl as a therapeutic agent, is never caused by arsenobenzene.

Ehrlich considered that the explanation lay in the fact that the first few doses of arsenobenzene destroyed the spironemas in the blood stream, the skin and the mucous membranes, leaving the inaccessible spironemas in the meninges, nerves and bony canals unharmed. Unassailed by immune bodies, these are free to produce symptoms. This explanation is probably the correct one for these phenomena disappear on further treatment with arsenobenzene and mercury.

6. *Cerebral Toxemia.*—"Hemorrhagic encephalitis" and "serous apoplexy" are the names given to this alarming and often fatal complication. Mild cerebral toxemia may occur and pass off. The

symptoms are limited to severe headache, slight rise of temperature and the patient may vomit. Hemorrhagic encephalitis, however, is a much more serious and more alarming condition. Unless recognized early and treated energetically it is invariably fatal. As a rule it follows the second injection of arsenobenzene but may occur at any stage under treatment. It commences by the patient feeling restless and often apprehensive about his condition without any apparent reason. The picture then rapidly develops; apprehension gives place to extreme nervousness. Headache, at first slight, becomes severe and edema of the face, vomiting and dyspnea supervene. Thereafter the patient becomes unconscious and signs of severe cortical irritation develop. The teeth are clenched and the jaw can be opened only with difficulty. Typical epileptiform convulsions may take place preceded by cyanosis, facial contortion and general twitching. These may be repeated at varying intervals and with varying severity. On the other hand, continuous convulsive movements of the face and limbs may be present all the time. The temperature rises to 104° F. in the evening, receding to 99° F. in the morning. Pulse is rapid, 140 per minute, usually of moderate tension and good volume. Respiration is rapid, deep and stertorous, but later shallow, feeble and irregular as the respiratory centre becomes exhausted. The Cheyne-Stokes syndrome may be present, but not invariably. Cyanosis is moderate and incontinence of urine and feces is present. The urine contains albumin, blood and, occasionally, sugar. At this stage death usually supervenes.

POSTMORTEM CHANGES.—Changes are most marked in the brain, liver, lungs and kidneys. These are the seat of extensive capillary damage with much extravasation of blood. In the brain the meninges may be engorged and disseminated punctate hemorrhages generalized. Capillary hemorrhages are less marked in the liver than in the other organs, while in the kidneys much extravasation of blood is found usually, around and into the tubules. The lungs may be engorged with blood and much interalveolar and interstitial extravasation may have taken place. On the other hand these organs may appear perfectly normal. Blood changes characterized by leukopenia, eosinophilia, and large lymphocytosis with destructive changes of the bone marrow have been observed by Moore and Foley.[10]

CAUSATION.—Explanations have been suggested by Ehrlich, Milian, McDonagh, Dudley and others. Ehrlich believed that the toxic action of paraminophenyl-arsenoxide (an oxidation product of salvarsan) and adrenal insufficiency were responsible for the condition. Milian has advanced the hypothesis that symptoms are due to the action of arsenic producing vasodilator effects in a patient suffering from adrenal insufficiency—hence the name "serous apoplexy" of the French school.

McDonagh has explained the condition as being due to the body's inability to deal with the toxins which result from the destruction of the spironemas. The system may cope successfully with the first flood of toxins but is overpowered by the second, thus explaining the occurrence of symptoms after the second dose. At this time the action of the toxins is an anaphylotoxic one, paralyzing the vasoconstrictor nerves. A general dilatation of the vessels results with extravasation of blood and edema chiefly in the brain, lungs and kidneys.

Dudley[11] believes that the most important causative factor is insufficient supply of oxygen to the tissues—anoxemia. Further explanation is provided by "the possibility of a breakdown in the mechanism controlling the hydrogen-ion content of the blood, which in turn prevents the respiratory centre from performing its function normally." Hitch[12] in reporting two fatal cases, concludes that "widespread capillary hemorrhages * * * afford a clear anatomical basis for the hypothesis put forward by Surgeon Commander Dudley that the symptoms are due to anoxemia, that this anoxemic condition is mainly produced by interalveolar hemorrhage into the lungs, and to a less extent by interstitial capillary bleeding into other organs."

Treatment.—The condition is an exceedingly grave one and usually fatal unless treatment is undertaken promptly. Even then it is not always successful. Since the cause of the condition is obscure, all available methods of treatment should be tried. They consist of the following:

1. Administration of oxygen. If the theory that anoxemia is the responsible factor is correct this measure is the most important one. Its administration should be continuous.

2. Intravenous administration of urotropin and caffein. The dose employed is 1.5 gram of urotropin and 0.2 gram of caffein in 15 c.c. sterile distilled water (Parnell). This causes extreme diuresis.

Parnell[13] reports a case treated successfully by a combination of these two measures after all other methods had failed to secure any signs of improvement.

3. Venesection. The removal of 18 to 20 ounces of blood is recommended in all cases, but particularly in cases of convulsions with coma.

4. Lumbar puncture will relieve intracranial pressure.

5. Washing out the stomach with magnesium sulphate and leaving sodium carbonate in it. This procedure is based on the assumption that there is an acidosis or an increased hydrogen-ion concentration as in shock.

6. The repeated injection of 1 c.c. doses of adrenalin hydrochloride 1 in 1000 solution. The rationale of this procedure lies in the adrenal insufficiency theory referred to above.

7. The use of bromides and other sedatives.

8. Purgation, and the large intake of barley water.

7. *Icterus.*—Jaundice as a manifestation of syphilis has long been recognized. Paracelsus in the sixteenth century is believed to have been aware of its significance. Gubler described five cases in 1853 and Wilks recognized its luetic origin in two cases which he reported in 1867.

Syphilitic jaundice, however, is a rare occurrence. Weiner (1897) met with it in 0.37 per cent of his cases, Scott and Pearson[14] (1919) in 0.11 per cent, and Hallam (1920)[15] in 0.12 per cent of cases.

Icterus following the administration of arsenobenzene was first reported by Klausner in 1911 and numerous cases have been reported by Pulvermacher,[16] Fabry, Friedmann, Fenwick, Parnell, Nicaud,[17] Ffrench,[18] Hallam,[15] Policard and Pinard,[19] Milian,[20] Golay,[21] and others.

Causation.—Two types of jaundice are met with, one due to the syphilitic process and the other to arsenical remedies. The first type occurs frequently before any arsenic has been administered; it is usually mild and clears up with treatment. Ffrench has suggested that it is due to a widespread fatty degeneration of the liver cells caused by toxins of spironemal origin.

Case 2.—The patient, aged twenty-three, slimly but cleanly built, was admitted with an advanced primary lesion situated at the frenum. Its duration was stated to be forty-four days and it had not been treated. Spironema pallidum was readily demonstrated and the serum Wassermann reaction was definitely positive. There was a well-marked icterus which had been fully developed for forty-eight hours but had increased gradually in severity for six days. The skin and conjunctivae were deeply pigmented and the itching and irritation were intense. There was no secondary rash, the mucous membranes were otherwise healthy and there was no pyrexia. Biluria and albuminuria were present but were slight. Treatment consisted of three doses of 3.0 c.c. intramine at four-day intervals, followed by 0.15 gram novarsenobillon intravenously every second day. The jaundice cleared up completely in 24 days. In this time he had received 9.0 c.c. intramine and 0.9 gram novarsenobillon.

The second type of jaundice is due chiefly to the arsenic, but in addition the syphilitic degeneration of liver cells may play a part [Ffrench,[18] Scott and Pearson[14]]. The bulk of the evidence goes to show that the arsenic and not the benzene group is responsible chiefly. Strathy, Smith and Hannah[22] report a clinically identical case of jaundice which followed treatment with Fowler's solution. That the luetic process plays only a small part is suggested by three cases of arsenobenzene jaundice which occurred in patients who were not suffering from syphilis reported by Golay.[21] Similar cases have been put on record by Pulvermacher,[16] and by Zimmern.[23] Ffrench[18] believes that exposure to cold is an important predisposing factor in all his cases. The writers, however, while not minimizing the importance of this, have seen cases where this element could be definitely excluded.

Arsenobenzene icterus may be divided into three groups:

(a) Icterus closely following an injection of arsenobenzene and due, possibly, to the Jarisch-Herxheimer phenomenon.

(b) Icterus due to the toxic effect of arsenobenzene acting on a liver already impaired by diffuse hepatitis. The dose of arsenobenzene is not a large one and, had the liver been normal, would not have been sufficient to cause an icterus. These cases occur during treatment and are mild in character but chronic in duration.

(c) Icterus due to overwhelming toxicity of arsenobenzene acting on a normal but overtaxed liver. These cases occur late in treatment, and may be seen in nonsyphilitic patients. As a rule they are exceedingly severe.

Hallam[15] thinks that the possibility of an infection resembling Weil's disease (spirochetosis icterohemorrhagica) must be considered a possible etiological factor. The occurrence of arsenobenzene icterus as an epidemic in 1917-18 lends color to the suggestion, especially since it was proved that no particular batch or issue of drug was responsible. This possibility is discussed also by Silbergleit and Fockler[24] who, however, do not offer an opinion. There is much evidence to support the view that causes other than those of spironemal or arsenical origin are extremely liable to be overlooked.

Lynch and Hoge[25] look upon concomitant mercury as an etiological factor of importance. They consider the cause to be a toxic action of arsenic on the liver combined with faulty elimination of the drug. The latter results from a mercurial nephritis. Thibierge also considers renal insufficiency a factor. Foulerton,[26] commenting on his series of animal experiments, remarks that the action of mercury on a liver already impaired by the toxic action of arsenic should receive further investigation.

SYMPTOMS.—The onset of jaundice is usually preceded by one or more attacks of vomiting and if arsenobenzene is continued, by chills, pains and cramps in the legs, pain in the right lumbar region, tenderness over the hepatic area, eye pains, constipation, and rise of temperature accompanied by severe headache. As already indicated, warning signs of an onset are chronic headache, anorexia, insomnia, general lassitude, malaise and loss of weight. Immediately before an attack there may be suppression of urine.

The clinical picture closely resembles ordinary obstructive jaundice. The prodromal symptoms, the urine and feces, and the course of the disease are very similar. Besides the pigmentation the chief symptoms are pruritus, pains in the eyes, digestive upset, nightmares, and loss of weight. The jaundice is well-marked and very persistent and the course of the disease is protracted.

In dealing with early syphilis the question of existing syphilis of the liver rarely complicates the diagnosis of the type of jaundice. This may crop up, however, with the possibility of arsenobenzene having a provocative effect on latent syphilis, calling it into activity. The behavior of the liver prior to treatment will usually suffice to eliminate other possibilities.

Jaundice due to the cumulative action of arsenic on an overtaxed liver occurring late in treatment may be exceedingly severe and even fatal. The onset is sudden with intense paroxysmal vomiting. The symptoms differ in no way from those already described except in their severity.

POSTMORTEM CHANGES

The Liver.—The liver is small, brownish in color, necrotic, and weighs only about 25 to 30 ounces (700-750 grams). There is evidence of extensive destruction of the liver due to a toxin of great virulence and large dosage. The center of the lobule is severely affected, the histological changes depending on the rapidity and severity of peripheral zone involvement. The destructive changes and necrosis are dominated by fatty degeneration, particularly when the process has been slow and prolonged. Where the termination has been rapidly and suddenly fatal there is little fatty change. The formation of lipochrome granules takes place in the cells at the center of the lobules and within the epithelium of the biliary ductules. Where the process is slow, some regeneration takes place in the cells at the extremities of bile-ductules. The character of the infiltration and the degree of fibroblastic proliferation serve as an index of the duration of the process. The lesions are not due to organismal activity, neither is there any evidence of spironemal damage. There is no accumulation of bile pigment.

Pierce classified arsenical lesions of the liver into three groups:

(1) The diffuse lesions which may be general or focal and show no preference for any particular region or structure of the lobule.

(2) Lesions of the central zone of the lobules including degenerative processes and necroses. These lesions differ in no way from those produced by a large number of other chemical agents.

(3) Lesions found in the structure of the portal space and the periphery of the lobule. With large arsenical doses necrosis of the structure is complete. With small doses the bile ducts suffer most while the degree of fatty degeneration of the cells at the periphery is slight.

The Kidney.—The kidney as a whole is small and weighs 4½ to 5½ ounces (128-156 grams). The cortex is swollen and pale and the capsule strips normally. There is severe parenchymatous degeneration dominated by fatty changes. Hemorrhages into the tubules and the interlobular tissue are frequent.

The Spleen.—This organ is large, soft and pale and weighing 7 to 8 ounces (191-220 grams). Signs of general subacute inflammation are present with central necrotic changes in the Malpighian bodies.

The Lungs.—Unlike these organs in hemorrhagic encephalitis the lungs as a rule show no pathologic changes, but sometimes a few subpleural petechiae and hemorrhages are present.

The Heart.—Here one may meet some fatty degeneration. Small subpericardial hemorrhages are often found. Any inflammatory reaction is always small.

Intestine.—Submucous hemorrhages in the stomach and the intestine are characteristic. These may be the direct result of the poison or simply due to toxins resulting from hepatic insufficiency.

Treatment.—Icterus is a signal to cease treatment with arsenobenzene at once and it should not be resumed until the skin, urine, and feces have been normal for a month.

By far the best remedy at our disposal is intramine-diorthodiamino-thio-benzene. Its usefulness has been recorded by Ffrench and the writers have employed it with success in a series of 14 cases. Its action may be intensified by the concomitant use of iodine. The dose is 2.5 c.c. given intramuscularly. In mild cases two or three doses are sufficient, repeated at three or four day intervals. In severe cases, however, as many as twelve doses may be given at similar intervals. We have no theory to offer as to its mode of action; it has been said to act as a reducing agent. The drug acts quickly and the pain at the site of inoculation usually is infinitesimal although occasionally considerable stiffness and local discomfort may be experienced. A rise of temperature frequently follows the injection. The patient himself feels more comfortable afterwards and several times we have found patients asking for another dose because they were satisfied that "it did them good."

Rest and careful diet combined with no further administration of arsenobenzene usually effect a cure. The bowels should be kept active and plenty of bland fluid given. It is important to avoid the use of calomel. Since arsenic is allied to mercury in its damaging effect on the liver it is clear why calomel should not be employed. If intramine is included in the scheme of arsenobenzene treatment the possibilities of a toxic jaundice occurring are reduced.

8. *Dermatoses.*—Urticaria or a simple itching of the skin following an injection of arsenobenzene is not uncommon. It is a sign of intolerance and should be regarded as such. More serious, however, is an erythema usually of the punctate or morbilliform type with high pyrexia. In some cases the rash might easily pass for scarlet fever and in others for German measles. Most cases are

mild and clear up quickly and spontaneously but severe types may go on to desquamation.

A more severe form is an exfoliative dermatitis which spreads all over the body. Mild cases tend to limit themselves to particular regions and in these circumstances exfoliation does not take place. When the rash becomes generalized one may take it that an exceedingly serious condition has developed and that, in every case, the patient's life is in danger. This exfoliative type occurs usually after the patient has received a large number of doses of arsenobenzene. It is rare for symptoms to come on later than a month after completion of treatment. On the other hand we have seen on two occasions fully developed exfoliative dermatitis happen after a single dose. The brand of arsenical preparation does not seem to matter, for a greater incidence of dermatitis cannot be laid to the charge of one preparation any more than of another. The incidence, however, is fortunately rare. Illustrative cases have been reported by Ffrench,[18] Parnell,[8] Strathy, Smith and Hannah,[22] Rawlins,[27] H. A. Jones,[28] Oltramare,[29] Leonard,[30] and others.

The eruption usually starts on the flexor aspect of the forearms, next appearing on the face. In a very short time it spreads all over the body. At first it appears as a dark-colored scarlatiniform rash which rapidly becomes confluent. Small vesicles appear in the folds behind the ears, at the sides of the nose and on the neck. Blebs and pustules form all over the body, and their rupture causes crusting and scaling. Itching is very troublesome and is a source of infinite annoyance to the patient. There may be complete loss of hair on the scalp and shedding of the eyelashes and eyebrows.

There is very extensive exudation into the skin and a characteristic puffiness and swelling of the face and head. The eyelids become so swollen and the face so puffy that the malar eminences practically meet the eyebrows, the eyes have disappeared from sight and the patient is unable to see. The conjunctivae are very infected and inflamed, the eyes feel sandy and lacrymation and photophobia are exceedingly troublesome. Transient blindness with edema of the optic discs may occur.

A weeping eczema is usually present behind the ears, at the nasal folds and folds of the eyelids, and involving the lips, axillae, pubis, scrotum and perineum. Pyemic abscesses are common in severe cases and appear with alarming rapidity and persistence. Adenopathy is general and well-marked and occasionally the glands in the axillae break down.

The skin at first becomes lobster-red and later reddish-brown. As exfoliation starts the skin settles down to a deep brown pigmentation and becomes thin and atrophic. The puffiness and general oozing and pain in the half-closed eyes and the very severe itching of the skin cause loss of sleep and the patient's health is soon seriously affected.

In some cases constitutional symptoms may be slight but as a rule they are exceedingly severe. There is a high pyrexia accompanied by persistent headache, diarrhea, retching of most trying severity and vomiting of bile-stained material. The tongue is dry, brown and heavily coated and the patient passes into the typhoid state. He is delirious and restless and often, if not closely watched, will get up and stagger about the room.

In severe cases it is not unusual for the eruption to become hemorrhagic in places after the dermatitis has progressed for some time. When this happens the adenopathy is well-marked and the glands particularly liable to break down.

Lung complications are particularly fatal; pulmonary edema and bronchopneumonia are frequent complications in fatal cases.

The patient becomes very emaciated and bed-sores are often trying and difficult to avoid or keep clean. Recovery is slow and convalescence protracted. When exfoliation is progressing the bedclothes are one mass of dry flakes and scales of considerable size. The skin thereafter is glazed, bronzed, thin, and atrophic. Later it assumes a beautiful pinkish hue. The patient's appearance is so changed that his own friends may fail to recognize him. His features seem to have lost their proportion and he looks like an entirely different person. He returns to normal, however, in a month or two. The appetite returns sooner than one might expect and very often the patient will eat voraciously. Depression is a characteristic feature and often persists after the patient is eating well. Hyperkeratosis of the palms and soles frequently develops and these are the last to desquamate. Thick epidermal plates come away late during convalescence.

CASE 3.—Private R. L., age twenty-three, under treatment for primary syphilis, had received 8 weekly intravenous injections of galyl in 0.3 gram doses together with 6 weekly injections of 1 grain doses of metallic mercury. These were taken without incident. He was a strong, well-built, vigorous young soldier and on no occasion had he shown any sign of idiosyncrasy or intolerance. During treatment he had gained 13 pounds in weight. On completion of treatment he weighed 179 pounds, his Wassermann reading, formerly positive, was now completely negative, and his urine was always albumin free.

Forty-eight hours after the eighth injection he complained of severe headache and feeling of ''general weakness.'' On examination a slight erythema was made out on the flexor aspect of both forearms; on the following morning this had spread to the face. In a very short time a typical dark-brown measly eruption had spread all over the body, the face and head were already swelling and the tongue was coated. There was albumin in the urine in small amount. Blebs and papules quickly made their appearance and the rash now was becoming confluent.

There was a high pyrexia and the patient was extremely ill. He was delirious and restless and got up and walked down the corridor where he was found and was with difficulty returned to bed. His condition now was alarming and the delirium increased. A second time he got up and wandered about and a special orderly had to be detailed off, day and night, to restrain him. On the sixth day he had to be forcibly held down in bed by two orderlies and he made continuous struggles to get up for thirty-six hours. The urine was scanty and loaded with albumin.

Treatment so far had consisted of purgation, milk diet, ichthyol internally—5 minims being given in cachets three times daily, four hourly 10 minim doses of 1 in 1,000 adrenalin hydrochloride, and calamine cream applied externally. In the first few days he had complained of feeling cold so extra blankets had been issued and a fire was put on in his room.

On the sixth day a supply of intramine was wired for, and he received 3.0 c.c. on the evening of the seventh day. This was repeated three days later, and the ichthyol was discontinued. The patient seemed to settle down after this dose and the facial exudation subsided perceptibly. The acute stage now seemed practically over, the temperature came down and exfoliation commenced. Intramine was repeated every four days up to the thirty-first day. The bed was a mass of scales and had to be cleansed several times daily. The patient was quite unrecognizable and his complexion rivalled that of any young girl. Recovery was slow but straight-forward and he was discharged from hospital on the fifty-seventh day. His general appearance was returning to normal, his appetite was good, his urine albumin-free and he weighed 161 pounds.

PROGNOSIS.—The prognosis is usually favorable if the condition is recognized early and arsenobenzene discontinued at once. It is frequently the case, however, that patients notice a slight erythema but are so anxious to be cured that they conceal it in case the next dose may be withheld.

The condition is always a serious one and the patient's life must be considered in danger. Should lung complications supervene, the outlook is well-nigh hopeless. Since employing intramine as a curative measure, the prospects are much brighter.

The following unusual case, however, indicates how uncertain any prognostication may be:

Case 4.—The patient was a healthy man but undersized and slightly built. He was forty-one years of age, and his medical category was B.2. He had been treated for secondary syphilis, receiving 3.9 grams of neo-kharsivan intravenously and grains 7 metallic mercury intramuscularly, extending over a period of 56 days. This he underwent without incidence. His urine was free from albumin throughout the course. On the fifty-eighth day his Wassermann reaction which had originally been strongly positive, gave a complete negative result. He was forthwith prepared for discharge from hospital.

On the morning of his discharge (the sixtieth day) he complained to me of having a headache and general discomfort. On examination it was found that a scarlatinal eruption had appeared over both forearms on the flexor aspect. His temperature was 102° F. He was re-admitted to the ward, put to bed and adrenalin 1 in 1000 administered in 10 minim doses every four hours. Calomel followed by a saline was given.

This became a severe case of arsenical dermatitis. The temperature remained at 102° F. He became progressively worse in spite of 5 minim cachets of ichthyol thrice daily; calamine cream and bran baths gave very little or no relief and he became worn out with discomforts and loss of sleep. The ichthyol was discontinued on the eighth day as it seemed to be quite ineffective. On this day 2.5 c.c. intramine was given intramuscularly. The following day the temperature dropped to 99.4° F., the patient expressed himself as feeling better and exfoliation commenced over the face and forehead. There was no pain at the site of injection and no local reaction. Exfoliation continued and four days later a second injection of 2.5 c.c. intramine was given, again causing no local pain. The skin exudation had now gradually subsided and exfoliation had continued apace. A third and a fourth injection of intramine were given in similar doses at four-day intervals, and the patient steadily improved. The skin became an intense reddish-brown tint and the itching was very severe. This gradually subsided and the skin was left very thin and atrophic and of a deeply pigmented dull coppery hue. The patient's general condition steadily improved, his voice was stronger, he became interested in his surroundings, his appetite improved and he became much less depressed.

On the twenty-seventh day a very large noninflamed swelling appeared suddenly at the lower end of the sternum in much the same manner as an abscess. By evening it had reached the size of a cricket ball. There was no surrounding inflammation and no "pointing." The following day similar smaller swellings had appeared over the external condyle of the left femur, the upper third of the left fibula, over the symphysis pubis, the upper third posterior aspect right thigh, the external surface upper third of the right tibia, the left epigastrium, the back of the left elbow and on the sacrum. They varied in size from a walnut to a large plum. These were fluctuating, noninflamed but painful swellings. They seemed peculiarly tender, ordinary gentle palpation being resented by the patient. The contents appeared to be a slightly opalescent, thick gelatinous, stringy, mucinoid substance which was very difficult to draw into a syringe even through a needle of large lumen. No pus cells or organisms were present. These swellings continued to appear, until by the fifty-first day they increased in size, remained for two or three days, then burst and healed over in twenty-four hours without a scar. The patient steadily lost weight but otherwise maintained his general condition. He did not look ill and his voice was that of a strong healthy man.

The tumor formation continued without abatement and, owing to lack of nursing facilities, he was transferred to a general hospital. There he lost ground insidiously and the case terminated fatally a few months later. The postmortem finding coincided with that condition described as acute yellow atrophy.

It is extremely difficult to suggest any cause for this extraordinary process of tumor formation. Pyemic abscesses containing definite pus occur in severe cases of ''606'' dermatitis. Here, however, the absence of pus and the sterility of the tumor contents, together with the noninflammatory nature of the swelling makes it extremely difficult to draw any comparison. The process seemed to be of the nature of a subcutaneous myxomatous degeneration. (This case was reported in *The Lancet,* September 13, 1919.)

TREATMENT.—The treatment of exfoliative dermatitis is often very difficult. The diet should be of the simplest character, consisting chiefly of milk and soda, milk and lime water, milk puddings and gruels. Meat and eggs are not indicated. The patient should be given plenty of fluids. A daily bran bath should be given and crusts removed with boric starch poultices. Should abscesses burst or glands break down, they should be kept clean and dressed with simple boric or eusol dressings. If the eruption is merely erythematous calamine lotion or powder should be used, while ichthyol up to 10 per cent, either with calamine liniment or zinc paste, should be applied if there is pustulation. Two or three drops of a 25 per cent argyrol solution dropped in the eyes night and morning will ease the conjunctivitis. This should be followed by a boric solution eye bath.

The patient complains of feeling cold and every precaution should be taken to prevent chills. The mouth should be looked after most carefully, and special care taken of the face and eyes. The swelling of the eyelids is very trying and the constant lacrimation and oozing of the eyes generally require very constant attention. A nurse should be always within call otherwise the patient may get out of bed and catch a chill.

In cases of severe headache and hyperpyrexia venesection and the withdrawal of 10 to 20 ounces of blood often will abort or relieve severe symptoms. It should be tried in every case.

When dealing with this condition our stand-by is intramine. Since its introduction the duration of these cases has been reduced by 50 per cent. Ichthyol in 5 minim doses given in cachets thrice daily has been advocated, but we have not seen results which compare favorably with those secured by intramine medication. The dose is given intramuscularly, 2.5 c.c. of a 1 per cent emulsion being used. If combined with collosol iodine, its action is enhanced, therefore it is well to incorporate three or four intravenous doses of collosol iodine in the scheme of treatment. A suitable dose is 50 to 100 c.c. Intramine acts very quickly and even the patient usually expresses his appreciation of its immediate benefit. The discomfort at the site of injection is usually small. Indeed one has administered this drug in the most emaciated patients without eliciting complaint. The temperature may rise a little in the evening following the injection but it comes down again towards morning. As many as twelve doses may be given. While in most cases the benefit of the drug is most marked, cases occasionally occur where its administration fails to evert a fatal termination. Success has been recorded by Ffrench[18] and by Rawlins[27] and failure by one of us.[31] An instructive case of exfoliative dermatitis complicated with cellulitis obliterative arteritis and gangrene of the toes has been put on record by H. A. Jones.[28]

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Abstract of
Current Syphilis Literature

It is the purpose of this Journal to review so far as possible all literature on syphilis as it appears in other medical periodicals and to present it in abstract form. Authors are requested to send abstracts or reprints of their papers to the Associate Editor, Dr. Grayson E. Tarkington, Dugan-Stuart Bldg., Hot Springs National Park, Ark.

GRAYSON E. TARKINGTON, M.D., EDITOR.

Syphilis in Hospitals for the Insane: Its Diagnosis and Treatment. H. W. Mitchell, Warren, Pa. The Therapeutic Gazette, 1922, vol. xlvi, p. 546.

Syphilis is probably responsible for more cases of insanity than any other preventable cause. Since the discovery of the Spirochaeta pallida as the infective agent of syphilis, numerous laboratory methods tending to promote accuracy in diagnosis have been accepted as reliable aids in differentiating neurosyphilis from other cerebral disorders. They should not be used to the exclusion of history and neuropsychiatric examinations, which are as valuable and necessary as formerly. Serological tests unquestionably make the diagnosis in cases that for a time, at least, would otherwise escape detection. They contribute immeasurably to early diagnosis and should be used in routine for all new admissions to hospitals for the insane. On the other hand, cases of paresis have been reported which have gone to autopsy with confirmation of diagnosis, showing negative findings in both blood and fluid, upon repeated examinations. Whatever favorable results, temporary or permanent, may follow treatment of the insane neurosyphilitic, the first efforts for control of the condition must be made by others than the hospital physicians. There must be competent board of health supervision of syphilitics to insure adequate treatment and prolonged supervision of all cases, with control of the sources of infection. Treatment of infections should be prompt and thorough upon diagnoses established, when possible, before the appearance of constitutional symptoms. Blood and fluid tests should be used at intervals throughout the lifetime of syphilitics and treatment pushed vigorously when indicated.

Transmissibility of Syphilis in the Latent Stage and Insufficient Treatment of Early Syphilis.—Samuel Feldman, New York City. New York Medical Journal and Medical Record, 1922, vol. cxv, p. 512.

Two cases were discussed. From case number 1, it was concluded: That a secondary eruption may recur in cases that have not received sufficient treatment. That a fresh systemic invasion may take place not only in cases where the secondary eruption has been suppressed by a subcurative course of treatment, but also in cases where the subcurative treatment has been started after the appearance of the secondary eruption. In this case the second eruption is called a recurrent secondary. From case number 11, it was concluded: That a latent syphilitic may infect others, in this case after having been symptomless for seven years. That a negative Wassermann reaction in an asymptomatic patient in the presence of a syphilitic history means nothing. That a negative reaction in a syphilitic may and frequently does revert to the positive after a certain amount of treatment. It tends to corroborate the law of Profeta, in so far that a syphilitic mother may give birth to asymptomatic children, but no conclusions can be drawn as to whether a syphilitic mother can give birth to nonsyphilitic children. It is unfortunate that the two children mentioned above have not been long enough under observation to determine the presence or absence of syphilis.

The Excretion of Spirochaeta Pallida through the Kidneys.—Alfred S. Warthin, Ann Arbor, Michigan. The Journal of Infectious Diseases, 1922, vol. xxx, p. 569.

Spirocheturia appears to be a striking phenomena of the entire group of spirochetal infections. The elimination of the spirochetes through the kidneys with the production of associated renal lesions appears to constitute a family characteristic in so far as the known types of the organisms have been studied thoroughly. It is best known in the case of infectious jaundice, and in this disease is a factor of considerable diagnostic value. Syphilitic spirocheturia occurs in the stage of septicemic syphilis, in both the congenital and acquired infections. Spirocheta pallida, as is Spirocheta icterohemorrhagica, may be excreted in enormous numbers through the convoluted tubules. During such excretion through the kidneys the spirochete of syphilis suffers greater destruction than does the icterogenic parasite, so that fewer spirochetes may reach the urine in syphilis than in infectious jaundice. The demonstration of the occurrence of syphilitic spirocheturia, is, therefore, not likely to possess such diagnostic value as that of icterogenic spirocheturia. It seems probable that spirocheturia is more likely to occur when the spirochetes in the blood stream are exposed to the action of antibodies or spirocheticidal drugs. Further, spirocheturia in any degree, both in the case of syphilis and infectious jaundice, appears to be associated with definite degenerative lesions of the epithelium of the convoluted tubules. Such lesions may make the tubules more previous to the passage of the spirochetes.

Bacterial Endocarditis as a Sequel to Syphilitic Valve Defect.—LeRoy H. Briggs, San Francisco. American Journal of the Medical Sciences, 1922, vol. clxiv, p. 275.

A case is reported of an individual suffering from a typical syphilitic aortitis and aortic endocarditis. One year later the patient enters the hospital with a nonhemolytic streptococcic endocarditis, which pursues the usual course and terminates in death. At necropsy a characteristic syphilitic aortitis with involvement of the aortic ring is found, together with an acute verrucose endocarditis of all the aortic cusps and perforation of one, with an extension into one mitral leaflet.

A Specialized Favoid Scalp Condition Peculiar to the Syphilitic Native of South Africa.—A. Reith Fraser, Capetown, S. A. The British Journal of Dermatology and Syphilis, 1922, vol. xxxiv, p. 267.

Wit kop is the name given to a favoid scalp condition which is prevalent among syphilitic natives in Bechuanaland. The bulk of evidence goes to suggest that it is a specialized papul-pustular syphiloderm characteristic of heredosyphilis in the Bechuanaland native, but occurring coincidently with the secondary eruption in adult native syphilis elsewhere. A fungus of the Achorion schonleinii type has been isolated from wit kop scalps of very long duration. Mice are readily infected with this fungus and an exceedingly irritative lesion is produced. Since wit kop is essentially a noncontagious, nonirritative process, it seems unlikely that such a spore growth is an etiological factor of importance. The condition has never been met with in a European, nor in a nonsyphilitic native. It occurs but seldom, and atypically, in the coastal bastard races. Untreated cases run a slow, chronic, unresolving course, with a marked tendency to relapse. Cases treated with arsenobenzene and mercury respond rapidly.

Congenital Syphilis and the Eruption of the First Teeth.—Ellsworth Moody. Joplin, Mo. The Journal of the Missouri State Medical Association, 1922, vol. xix, p. 295.

Three cases were presented. These cases seem to indicate that congenital syphilis may be an even more important cause of failure of the first teeth to erupt than rickets and that the disease may cause no changes whatever in the shape, size, arrangement or interfere in any way with the enamel formation of these deciduous teeth even when the inhibition of eruption has been to a marked degree.

Neurosyphilis.—H. Butts and W. M. Alberty, United States Navy. United States Naval Medical Bulletin, 1922, vol. xvi, p. 483.

Involvement of the nervous system occurs at an early period of the disease. Early diagnosis and treatment are necessary to prevent later and more serious complications, such as paresis and tabes dorsalis. Spinal puncture should be made routine in every case of syphilis as early as the diagnosis is made, regardless of stages, and certainly before discharging the patient as cured. Many cases remain undiagnosed because of repeated negative blood Wassermanns, and in whom no examination of the spinal fluid has been made. No persistent case should be discharged from treatment until the intraspinal or intraventricular therapy has been instituted and strenuously administered.

Ulcerating Granuloma (Granuloma Inguinale). Mihran B. Parounagian and Herman Goodman, New York. Archives of Dermatology and Syphilology, 1922, vol. v, p. 597.

The chief points of interest in this case are: the patient was a white man, born and reared in New York City. He undoubtedly had tertiary syphilis. He had lesions of ulcerating granuloma, of Donovan-body origin, of the groins, anus, and surrounding parts, with cicatrization, and edema of the penis and scrotum. In addition, he presented similar lesions of the upper lip and the side of the neck. He showed also a smooth, glossy atrophy of the tongue. Silver arsphenamine and neoarsphenamine were of little benefit. The patient has not returned for treatment with tartar emetic.

Pre-Ataxic Gastric Crises of Tabes.—Clyde Fishbaugh, Los Angeles, Cal. California State Journal of Medicine, 1922, vol. xx, p. 53.

Gastric crises are often the first symptoms of locomotor ataxia and may remain so for years. Two of these cases had had definite stomach crises for fifteen years, one for six years and the other for four years, and none had shown ataxic signs. Until the symptoms of gastric crises are kept constantly in mind, and until the Wassermann test becomes routine in chronic abdominal complaints, spinal syphilis will continue to be mistaken for real abdominal pathology.

The Relation of Syphilis to Diagnosis and Surgery.—Albert M. Crance, Geneva, N. Y. New York State Journal of Medicine, 1922, vol. xxii, p. 357.

There are three necessary procedures in order to arrive at a diagnosis of obscure syphilis. First, a carefully taken history should be the introduction of every case. Secondly, the physical examination should include every part of the body, from head to foot. Thirdly, the taking of routine Wassermanns is absolutely necessary, and when occasion suggests, a provocative test should be taken. To this may be added the therapeutic test. The fact remains that there is an important relation between syphilis, diagnosis and surgery. The fact that syphilis may mimic all other diseases is sufficient to warrant the most careful consideration of all cases.

Syphilis in General Practice. Sir D'Arcy Power, England. The Lancet, London, 1922, vol. ccii, p. 1035.

The subject is considered under the following heads. Mistakes due to:—The unlikelihood of infection owing to the social position of the patient or the unusual mode of infection. Prolonged latency of symptoms generally in connection with inherited syphilis, as in cases where the patient has no stigmata, has married, and has had healthy children; or in the acquired disease, where very many years have elapsed since the patient had any signs. Under both conditions increasing age or slight injury appears to be the determining cause of the syphilitic manifestation. The modifying effect of syphilis on other forms of infective inflammation, whether it be tuberculous, phagedaenic, streptococcal, or staphylococcal. Syphilis affects a sufficiently large number of the population to make it worth while to bear in mind the possibility of a spirochaetal factor in many of the obscure and chronic inflammations which do not respond to the ordinary methods of treatment.

The Clinical Aspect of the Initial Lesion of Syphilis in the Male.—N. M. Gibson and C. J. Wiley, Sydney. The Medical Journal of Australia, 1922, vol. i, p. 123.

It is possible to make an accurate diagnosis of the primary syphilitic sore by clinical means alone in the great majority of cases. Direct microscopical examination of the sore is of considerable, but not primary importance, being to some degree limited in its applicability and not invariable in its results. It is, however, sometimes the only method by which the nature of a syphilitic sore may be recognized. Thus, it should always be employed, for it is obvious that the only sound method of diagnosis is to use with the knowledge that comes from experience, all the means available, both clinical and pathological. If direct microscopical examination of the sore does not reveal the spirochaete in a case definitely conforming to one or other of the clinical types, it is unjustifiable to wait for the appearance of the serological reaction; treatment should at once be instituted.

Venereal Spirochetosis in American Rabbits.—Hideyo Noguchi, Baltimore. The Journal of Experimental Medicine, 1922, vol. xxxv, p. 391.

Of 50 rabbits, otherwise regarded as normal, three adult females and two adult males (10 per cent) have been found to have in their genitoperineal region certain papulosquamous, often ulcerating, lesions. A recently purchased group of twenty rabbits contained six females (30 per cent) with similar lesions. This condition runs a chronic course and is characterized by the presence of a spiral organism closely resembling Treponema pallidum. The rabbit spirochete has the same morphological features as Treponema pallidum; it is possibly a trifle thicker and longer than the average pallidum. Long specimens measuring 30μ are frequently encountered, and they show a tendency to form loosely entangled knots. A stellate arrangement of several organisms in a mass is frequently observed. In the lesion of one rabbit there were two types of spirochete, one of the variety just described, the other a somewhat coarser organism, closely resembling Treponema calligyrum found in a human condyloma, but a trifle thinner and longer. This organism is perhaps merely a variant type of the rabbit spirochete. The histological reactions are similar to, but considerably less cellular, than those occurring in typical primary syphilitic lesions. There is a marked hyperkeratosis and interpapillary infiltration not observed in scrotal chancre. The disease is transmissible to normal rabbits, in which the usual papular lesions can be readily reproduced in the genitoperineal region. In the first passages the incubation period varied from 20 to 88 days; subsequently one of the strains produced a lesion in 20 days on the second, and in 5 days on the third passage. No typical orchitis or keratitis was produced in the rabbits of the present series, although in one of the original rabbits scaly, papular lesions have developed on the nose, lips, eyelid and paws. Monkeys (Macacus rhesus) failed to show any lesions within a period of 4 months after inoculation. In one instance transmission was accomplished through the mating of an infected female with a normal male. The Wassermann reaction was uniformly negative in the five rabbits with spontaneous lesions and in eighteen rabbits experimentally infected. Salvarsan had the same therapeutic effect on the lesions produced by the rabbit spirochete as on the experimental pallidum lesion of the rabbit. The organism belongs to the genus Treponema, and may be designated Treponema cuniculi.

The Staining of Spirochetes in Cover-Glass Smears by the Silver-Agar Method.—A. S. Warthin and A. C. Starry, Ann Arbor, Mich. The Journal of Infectious Diseases, 1922, vol. xxx, p. 592.

The authors believe that their method of demonstrating spirochetes in cover-glass smears by silver-agar silver impregnation is the surest and safest diagnostic method yet devised. It should replace the use of the dark-field and the India-ink method in the diagnosis of syphilis. The morphologic details of Spirochaeta pallida and the mouth and smegma organisms so often mistaken for it by workers using the dark-field or India-ink method are so accentuated that differential diagnosis is made much easier. The India-ink method is especially dangerous for inexperienced workers. The method is not formidable as it may seem because of the full directions given. It is easily acquired by laboratory workers. Aside from the time required for silver-impregnation in the incubator, it is a relatively short method, and a large number of smears can be kept going in different bottles at the same time. For bacteriologists and laboratory workers engaged in spirochete studies this method is of the greatest advantage in recovering organisms from the organs of inoculated animals, or from the blood or urine. It lends itself particularly well to the laboratory study of Sp. icterohaemorrhagica and Leptospira icteroides. Nevertheless it is in its application to the clinical diagnosis of syphilis that it possesses its greatest value.

Serologic Studies on the Exudate of Syphilitic Chancres.—Cesar Fuentes, Havana, Cuba. Archives of Dermatology and Syphilology, 1922, vol. vi, p. 136.

In the exudate from chancres which are clinically syphilitic there is a substance that acts as amboceptor in the Wassermann test. There has been found also in the exudate of the same chancres another substance that acts as antigen in the Wassermann test. In the exudate from chancres which are clinically negative with no spirochetes, no antigen or amboceptor has been found. While only one mixed chancre was studied, both antigen and amboceptor were found besides spirochetes. The substance that acts as amboceptor and the substance that acts as antigen were found together when their presence was demonstrated. While both substances appeared together, it has been possible to demonstrate their presence independently using the Wassermann test for this purpose. In all the exudates from the chancres examined which contained spirochetes both antigen and amboceptor have always been found. No case was positive for spirochetes and negative for antigen and amboceptor. Exudates from chancres that were clinically positive but in which no spirochetes were found contained both antigen and amboceptor. The amount of complement in these exudates is not sufficient to change the positive or negative reaction.

The Formalin Test for Syphilis.—A. G. Holborow, Gibraltar. The Lancet, London, 1922, vol. cciii, p. 275.

When serum forms a gel with formalin it is due to the direct action of the reagent upon serum albumin or serum globulin, or both, and not due to any action upon the toxins of Sp. pallidum direct. It is probable that acid-protein produces a gel with formalin and alkali-protein does not. If formalin forms a gel of human serum it is an indication of decreased alkalinity of that serum, but does not decide the cause of the decreased alkalinity. The evidence obtained from the foregoing experiments is, in my opinion, sufficiently adverse to regard the formalin test for syphilis with much reserve.

A Simple Quantitative Precipitation Reaction for Syphilis.—R. L. Kahn, Lansing, Mich. Archives of Dermatology and Syphilology, 1922, vol. vi, p. 332.

The method.—Measure with a 0.1 or 0.2 c.c. pipet graduated in hundredths cubic centimeter, two 0.03 c.c. quantities of serum into two agglutination tubes. With a similar pipet measure approximately 0.005 c.c. of diluted alcoholic antigen into one tube and the same amount of cholesterinized antigen into the other. The minute amounts of antigen should reach the serum in each case. Shake the racks vigorously for several minutes and incubate in the usual manner. The tubes should be properly corked to prevent evaporation. The results will be found to approximate closely those obtained with regular quantities. Table 2 gives a summary of findings with a small number of serums.

A Comparative Study of Three Colloidal Reactions on the Cerebrospinal Fluid.—D. O. Riddel and R. M. Stewart, Whittingham. The Journal of Neurology and Psychopathology, 1922, vol. ii, p. 325.

In a comparative study of spinal fluids in 30 cases of general paralysis the gold-sol test and the colloidal-benzoin reaction of Guillain, Laroche, and Lechelle gave parallel results; the gum-mastic reaction was in less close agreement. The colloidal-gold and the gum-mastic tests gave paretic curves in nonparetic fluids. The colloidal-benzoin test gave paretic curves only in paretic fluids. Syphilitic curves were obtained in all three tests from cases that clinically were not examples of neurosyphilis. In the colloidal-benzoin reaction a slight degree of precipitation in the middle series of tubes was often obtained with normal cerebrospinal fluid.

A Comparison of the Formaldehyd-Gel Reaction of Gate and Papacostas with the Wassermann Reaction.—Victor Burke, San Francisco. Archives of Dermatology and Syphilology, 1922, vol. v, p. 469.

The formaldehyd-gel test as used in these experiments is not so reliable a test as the Wassermann test with a cholesterinized antigen and water-bath incubation. It is not quite so reliable as the Wassermann test with an alcoholic extract antigen. The formaldehyd-gel test gives results in closer agreement with the negative than with the positive Wassermann tests. When the two tests disagree, a positive formaldehyd-gel diagnosis will be found to be correct in an undetermined percentage of cases; a negative formaldehyd-gel diagnosis will rarely be correct. The substance on which the formaldehyd-gel reaction depends is not present in the spinal fluid of syphilitic patients, or at least not in sufficient amounts to cause coagulation on the addition of formaldehyd. Incubation of the serums in unstoppered tubes increases the number of positive formaldehyd-gel reactions. The increase in the number of positive reactions accompanies and is probably dependent on increased desiccation. It will probably be found that inactivation, unless increased evaporation is prevented, also affects the percentage of positive formaldehyd-gel reactions. Heat, aside from the effect on dessication, does not increase the number of positive reactions. Serum to which a small amount of formaldehyd has been added does not coagulate on exposure to a boiling temperature in a test tube. The ice box temperature delays the coagulation of the positive serums. An increase in the amount of formaldehyd added to the serums increases the percentage of water and delays the coagulation of the positive serums. Suggestions are given for the interpretation of results obtained with the formaldehyd-gel test and for future research.

The Vernes Reaction.—Leon H. Cornwall, New York. Archives of Dermatology and Syphilology, 1922, vol. v, p. 433.

The physicochemical study of the reciprocal affinity between fine suspensions and blood serum has demonstrated that there exists, under certain conditions, an intimate correlation between a flocculent and a hemolytic phenomenon. This correlation has permitted the establishment of a method of measuring syphilitic infection, the precision of which is based on the accuracy of its physical regulation. The minutiae of the technic demand precise scientific conditions. There is, however, sufficient latitude to allow any one point to be slightly varied without producing a disturbing effect on the reaction, providing the other points are not varied at the same time. The results submitted are small in number and represent the preliminary studies during the process of becoming familiar with the technic. The technic is susceptible of more uniform regulation than is possible with the Wassermann reaction. It is based on principles that can be demonstrated by visible physical phenomena, whereas the Wassermann test still rests on a rather uncertain theoretical foundation. The actual performance of the test is comparatively simple when one is provided with the proper equipment. The reaction registers objectively certain humoral modifications that accompany syphilitic infection. It would seem justifiable, therefore, to denote the results by the term syphilimetry. It is emphasized that this test is not a modification of the Wassermann test, although final judgment may be suspended concerning the question as to whether or not they both depend on the same underlying colloidal phenomena. Its chief value lies, not in a single application to a given case, but in the graphic record secured from periodic examinations. The value of this procedure cannot be gaged by its comparison with Wassermann results, but by its application to clinical and pathologic observations.

Effect of Time Between Obtaining a Spinal Fluid and Making a Cell Count on the Result of the Count.—James Wynn, Boston, Mass. The Journal of Laboratory and Clinical Medicine, 1922, vol. vii, p. 273.

The cells in clear spinal fluids, collected in clean tubes and tightly stoppered, may in the absence of macroscopic pellicle, sediment, or web be safely counted if thoroughly mixed at any time up to at least fifteen hours. If the spinal fluid is not clear or becomes clouded, the results of counts at different times are apt to vary. It is desirable but not necessary for fluids to be collected in sterile tubes. Whether the fluids are kept at room temperature or in the ice box seems to be of little consequence. In two cases of meningitis, the thorough mixture of small quantities (0.2-0.5 gm. for 6 c.c.) of powdered sodium citrate with the fluids made it possible to duplicate the original cell counts (within the limit of technical error) at three and fifteen hour intervals. The procedure must be tried in a large series of cases before any conclusions are warranted regarding such citrating of fluids.

The Precipitin Test of the Arachnoid Fluid.—Clarence A. Neymann and Ludvig Hektoen, Chicago. The Journal of Nervous and Mental Disease, 1922, vol. 56, p. 16.

With this test and a cell count, it is possible to confirm a clinical diagnosis of general paresis. The authors believe the reaction is more accurate than the colloidal gold test. It is far simpler. The antiserums keep for some months in the ice box. It has been shown beyond a doubt that the protein increase of paretic arachnoid fluid is due to an increase of globulin, and that in many epileptic arachnoid fluids there is some increase in albumin.

The Euglobulin Group and Its Relationship to the Wassermann Reaction.—C. H. H. Harold, Royal Army Medical Corps. Journal of the Royal Army Medical Corps, 1922, vol. xxxix, p. 83.

The Wassermann bodies are solely contained in the euglobulin group and are capable of complete precipitation with this group by dilution acetic acid methods. The amount of precipitable euglobulin in syphilitic sera varies directly as the strength of the Wassermann reaction. This can be verified by opacity tests, estimation of bulk after centrifugalization and Kjeldahl estimations. As a test for syphilis dilution acetic acid methods have possibly a place in Clinical Medicine. By separation and concentration of the euglobulin group from a (plus) serum (equals 3 M.H.D. complement deviation), it has been possible to make a solution which with antigen deviates 12 M.H.D. of complement and is not anticomplementary. The Wassermann bodies are intimately bound up with the euglobulin group, but by careful treatment of a syphilitic serum with CO_2 and acetic acid it appears possible to separate out: (1) the main euglobulin group plus a fraction of Wassermann bodies; (2) a fine film of precipitate which has stronger deviating powers in proportion to its bulk than the whole euglobulin group and at the same time it is not anticomplementary. Precipitation methods employing ammonium sulphate do not lead to great concentration of the Wassermann bodies but result in marked anticomplementariness with the higher saturations. The hemolytic bodies in hemolytic amboceptor unlike the Wassermann bodies are chiefly contained in the pseudoglobulin group. In malaria, under certain conditions, bodies may appear in serum which belong to the globulin group and react in the same way as the Wassermann bodies.

Wassermann and Sigma Tests.—W. T. Collier, London. The Lancet, London, 1922, vol. cciii, p. 274.

The Sigma test is slightly more reliable and more delicate than the Wassermann. It is also less complicated. A reading of one to four Sigma units only must be regarded as doubtful. If obtained on more than one occasion, it is probably evidence of syphilis.

The Original Sachs-Georgi Reaction in the Tropics as an Indication for Diagnosis and Treatment of Syphilis.—W. Leslie Webb, Uganda. Journal of the Royal Army Medical Corps, 1922, vol. xxxix, p. 98.

The most effective antigen used at the author's laboratory has been Bordet-Ruelen's antigen. An opalescent antigen emulsion is more effective than a turbid emulsion. The clearest emulsion is obtained by blowing the antigen mixture from a pipette into the right amount of saline as quickly as possible. Better results are obtained with all the antigens usually used by reading the reaction after eighteen to twenty-four hours' incubation and twenty to twenty-four hours' at room temperature, than by reading directly after eighteen to twenty-four hours' incubation. Incubation at 43° C. gives cleaner-cut results than incubation at 37° C. Where the Sachs-Georgi reaction is being used alone, and is not corrected and controlled by the Wassermann reaction, more reliable results are obtained by using two or three different antigens for each serum. In the author's experience the Sachs-Georgi reaction, using both the Sachs-Georgi antigen and the Bordet Ruelen's antigen in each case, is of the utmost value as an aid in the diagnosis of doubtful cases of syphilis, and to a less extent as an indication of cure or for further treatment, and could be usefully employed in all countries where, from one reason or another, the performance of the Wassermann reaction is impracticable. Its technic is so simple and its requirements so few, that it is hard to imagine any place where this reaction could not be carried out easily. Its adoption as a routine in such countries would undoubtedly lead to the more accurate diagnosis and treatment of syphilis.

The Value of Spinal Fluid Examination.—Charles E. Kiely, Cincinnati. The Ohio State Medical Journal, 1922, vol. xviii, p. 339.

Lumbar puncture is a procedure of thirty years' standing, so extensively used in the last ten years as to make it a commonplace. It is without danger. It is indispensable for the differentiation of the common types of meningitis and equally so for certain types of syphilis. The colloidal gold test enables us to make a prognosis in the most hopeless form of nervous syphilis. The spinal fluid examination detects intracranial hemorrhage in many fractures and gives a pathognomonic appearance in constriction of the cord, which is almost synonymous with tumor. Spinal puncture affords the sole means of treating epidemic meningitis as well as a successful method in certain cases of syphilis refractory to intravenous treatment. It gives startling results in many cases of delirium tremens and relieves migraine; it is an aid to surgical procedure and offers a method for anesthesia. It should be employed without fear.

Changes in Reaction Accompanying the Precipitation of Colloidal Gold by Spinal Fluid (Lange Test).—Edwin F. Hirsch, Chicago. The Journal of Infectious Diseases, 1922, vol. xxx, p. 658.

The agglutination of colloidal gold particles by spinal fluid (Lange test) is accompanied by an increase in the alkalinity of the medium in which this reaction occurs. This change in reaction is similar to that observed on the agglutination of bacteria by homologous immune serum.

Nonspecific Cross-Fixation of Complement with Wassermann and Tuberculosis Antigens.—Anna Dean Dulaney, Columbia, Mo. The American Review of Tuberculosis, 1922, vol. vi, p. 192.

Eight of the 100 sera from known tuberculosis patients, who gave neither history nor clinical evidence of syphilis, yielded positive Wassermanns with cholesterinized antigen. Of these, 2 sera gave a one-plus fixation with alcoholic antigen. The others were negative. Of the 500 sera for routine Wassermann test, 23 sera giving positive Wassermanns also gave fixations with tuberculosis antigen, while 20 Wassermann-negative sera gave positive tuberculosis complement fixations. The 23 sera giving fixations with both Wassermann and tuberculosis antigens represented 3 active tuberculosis cases, 2 suspected tuberculosis cases, 15 persons with neither history nor clinical evidence of tuberculosis, and 3 cases of which the author could obtain no histories. Of the 20 sera giving negative Wassermanns but positive tuberculosis complement fixations, 7 were from active tuberculosis cases, 5 from suspected or treated syphilitic cases giving neither history nor evidence of tuberculosis, 7 from persons giving neither history nor evidence of tuberculosis, and 1 from a case where no history was obtained. Ten per cent of "normal" persons, giving a negative Wassermann, gave a fixation with tuberculosis antigen. Five per cent of the 500 sera gave a fixation with tuberculosis antigen when there was no history or clinical evidence of tuberculosis. The author's results tend to show that a positive tuberculosis complement fixation in the great majority of cases indicates an active tuberculosis. In the case of "normal" persons who give a fixation with tuberculosis antigen, there is always the possibility of an old or latent infection. The sera from known tuberculous cases, giving positive Wassermanns without history or clinical evidence of syphilis, are regarded as cases of nonspecific cross-fixation. When only a cholesterinized antigen is used, a positive Wassermann in active tuberculosis is not to be accepted without thorough investigation.

Standardization and Preservation of Complement Serum for Wassermann Test.—E. H. Ruediger, Bismarck, N. D. The Journal of the American Medical Association, 1922, vol. lxxix, p. 551.

The serums from different guinea pigs differ greatly in fixability and in hemolytic power. In order to obtain fairly uniform complement serum, the serums must be selected, the good serums being used and the poor serums rejected. Breeding only guinea pigs with good complement greatly improved the author's collection of guinea pigs for this purpose in three years. Any raw vegetables, such as potatoes, cabbage or carrots, prevent scurvy and are suitable for winter feed for complement guinea pigs. A mixture of raw vegetables gives the best results. The fixability of guinea pig complement was much better in winter than in summer, which may be due to the large quantity of grass fed in summer. Frozen complement serum kept below zero Fahrenheit in cold storage room remained active for eight weeks.

Studies of Cerebrospinal Fluid and Blood of Syphilitic and Normal Persons.—Charles E. Nixon and Koichi Naito, Minneapolis. Archives of Internal Medicine, 1922, vol. 30, p. 182.

Positive colloidal gold reactions are due to the presence of precipitating substances. Both precipitating and protecting substances are present in pathologic cerebrospinal fluid. Curves in Zones I, II and III are due to varying amounts and proportions of the precipitating and protecting substances. Albumin and globulin may possess both precipitating and protecting power. Ultrafiltrates of syphilitic and nonsyphilitic serums give curves that are more or less similar, but there tends to be a greater difference between the zones of reduction of the original and filtered serum in syphilitic than in normal cases. The protecting substance is decreased by ultrafiltration to a greater degree than the precipitating substance. Changes in the state of the protein modified precipitating and protecting powers. The salt solution used in the colloidal gold test partially neutralizes the protective action.

The Interpretation of the Wassermann Reaction.—Sydney Wallenstein, Baltimore, Md. New York Medical Journal and Medical Record, 1922, vol. cxv, p. 514.

The Wassermann reaction for all intents and purposes may be regarded as specific. Great care and careful judgment must be exercised in the interpretation of the results of the Wassermann test. A negative reaction may occur in a syphilitic due to the normal daily variation in the complement fixation power of syphilitic serum. Contaminated blood may give falsely positive reactions. Wassermann fast cases mean a grave infection and usually visceral or nervous syphilis. A positive reaction with the cholesterinized antigen only or with the ice box method of fixation are of value only with a history or symptoms of syphilis. The ingestion of alcohol previous to taking blood will render the reaction negative. A positive reaction is obtained in normal sera shortly after general anesthesia. Blood containing bile may give a positive reaction. A negative reaction in the newly born for a period of four months is of no value. A single negative reaction means nothing. In a suspected case a series of eight consecutive daily tests should be done.

The Clinical Value of the Kolmer Complement-Fixation Test for Syphilis.—Charles H. deT. Shivers, Atlantic City, N. J. Archives of Dermatology and Syphilology, 1922, vol. vi, p. 344.

The author has employed the Kolmer complement-fixation test for syphilis in 320 cases—some with a definite history of specific infection and presenting clinical evidences of syphilis, others with negative histories and presenting no signs or symptoms of syphilis. The new method has proved a very sensitive and reliable test, much more so than the old method, being frequently positive while the latter is negative. The new method has yielded earlier positive reactions in primary syphilis than other methods, and is much slower in becoming negative when the patient is under treatment than the old method. A negative reaction with the Kolmer method is of more value when giving a prognosis. The new Kolmer method has not yielded falsely positive reactions in nonsyphilitic persons. The method has been proved more valuable in aiding a diagnosis of congenital syphilis in obscure cases than the old method. The new method marks a distinct and valuable advance in the serum diagnosis of syphilis, being much more sensitive and at the same time yielding no falsely positive reactions.

A Precipitation Test for Syphilis.—C. Y. Wang, Hong-Kong. The Lancet, London, 1922, vol. ccii, p. 274.

The test has been practiced on 200 serums, and was controlled throughout by the Wassermann reaction. In 192 cases (96 per cent) a parallel result was obtained with the two tests. Discrepant results were found in eight instances, which consisted of three treated cases, three cases with a definite sign or history of syphilis, and two unknown. All the positive Wassermann reaction serums, numbering 73, were found to yield also a positive reaction with the precipitation test. Of the 124 negative Wassermann reaction serums, 119 were negative, 4 were positive, and 1 was doubtful to the sedimentation test. The four serums which reacted positively to the sedimentation test but negatively to the Wassermann reaction were obtained in two instances from treated cases, in one instance from a case showing active manifestation of syphilis, and from one unknown. The three doubtful Wassermann reaction serums gave in two instances a positive, in the third a negative precipitation test. The former belonged to a treated and a latent case.

A Comparison of the Colloid Flocculation Test (Dreyer-Ward Technic) with the Wassermann Reaction for the Diagnosis of Syphilitic Infection.—H. J. B. Fry, London. The Journal of State Medicine, 1922, vol. xxx, p. 396.

The colloid flocculation test (Dreyer-Ward technic) is a rapid, simple and efficient test for routine laboratory diagnosis. The colloid flocculation test is as sensitive as the Wassermann reaction in the case of sera, but is slightly less sensitive than the Wassermann reaction in the case of cerebrospinal fluids. The sensitiveness of the test is appreciably increased by incubation to twenty-four hours. False positive reactions from prolongation of the incubation period have not been a source of error. The clinical evidence is at present insufficient to determine whether the Wassermann reaction or the flocculation test is the better measure of the effect of treatment.

The Luetin Test in Latent Syphilis.—A. E. Van Nest, Detroit, Mich. The Journal of the Michigan State Medical Society, 1922, vol. xxi, p. 132.

The author has found luetin to be of a definite aid in the diagnosis of latent syphilis and feels that it should be used as routine as the Wassermann, in an effort to secure 100 per cent diagnosis of syphilis.

The Sigma Reaction for Syphilis.—A. F. Rook, London. The Lancet, London, 1922, vol. ccii, p. 118.

The Sigma reaction for syphilis described by Dreyer and Ward is much simpler in technic than is the Wassermann reaction. The results of the series here reported would seem to show that the results as regards blood serum tests in untreated cases are as good, or even slightly better than the results obtained by the Wassermann reaction, when judged from a clinical standpoint. The results obtained in the cerebrospinal fluid have not been so good as have the results of the Wassermann reaction. These cases are, however, so few that it is impossible to draw any inference from them. The test is easily standardizable, both as regards technic and reporting of results. Being a quantitative reaction it is possible that important information as to prognosis or the effect of treatment may result in the light of further knowledge.

A Simple Quantitative Precipitation Reaction for Syphilis.—R. L. Kahn, Lansing, Mich. Archives of Dermatology and Syphilology, 1922, vol. v, p. 734.

In this article the author records further observations in a precipitation test for syphilis which bears the author's name: (1) the preparation of antigen; (2) the dilution of antigen for the tests; (3) the preparation of serum for the tests; (4) the optimum quantities of serum and antigen to be used in the tests; (5) the temperature and time of incubation, and (6) the reading of results.

Serologic Changes in Neurosyphilitic Patients During a Period of Nontreatment.—H. Omar and P. H. Carroll, Mendota, Wis. Archives of Neurology and Psychiatry, 1922, vol. vii, p. 733.

The laboratory findings in a series of nine cases of late neurosyphilis remained practically unchanged during a seven month period of nontreatment.

The Wassermann Test.—L. B. Bull, Sydney, Australia. The Medical Journal of Australia, 1922, vol. 1, p. 172.

The Wassermann test is an empirical adaptation of a specific immunity reaction, but differs from such reactions in certain respects. As to the actual understanding and importance of these differences there is no general agreement. One view is that the Wassermann antigens now in use behave like specific antigens, because they are analogous to the disintegration products due to the spirochaetes and that the reaction, therefore, confirms to all essential principles which govern true immunity reactions. An entirely opposite view is that it is merely a nonspecific physical or colloidal test based on the anticomplementary property common to a large variety of substances and that the test simply depends on the physical properties of syphilitic serum, which are such that an anticomplementary effect is more readily produced with it than without normal serum. The former view is used to explain the assumed specificity of ''Wassermann substance'' in relation to syphilitic infection and the latter serves to justify the need for arranging the test as a quantitative differentiation between the anticomplementary capacities of the serum of syphilitic, ''border-line'' and normal persons. At present the subject is too obscure for confident interpretation. Stated briefly, the problem of the Wassermann reaction is as follows: Normal fresh serum or complement dissolves red corpuscles when they are acted upon or sensitized by their specific antibody. Complement as a hemolysin may be neutralized by substances termed antihemolysins, which are of various kinds, the most important being (1) specific antigen-antibody combinations, (2) nonspecific biological products, such as tissue extracts, normal serum or egg-albumin, and (3) chemical compounds, such as cholesterol. At least the second and third group and possibly the first act in producing a reaction in nonsyphilitic sera if not adequately controlled.

Incidence of the Wassermann Reaction in a Large Child-Caring Institution.—L. H. Barenberg, New York, and Philip Rosenberg, Syracuse. Archives of Pediatrics, 1922, vol. xxxix, p. 23.

A group of Jewish institutional children were tested for syphilis. They varied in age from a few days to 6 years, and were unselected. Many had a family history or pathological conditions which would warrant a suspicion of syphilis. Eight hundred and thirty Wassermann tests on 472 children were performed by the laboratories of the Department of Health of New York City, as well as that of the State. Without exception they proved to be negative. Three hundred and ninety-nine luetins were performed on 350 of these children. Three hundred and twenty-one reacted negatively, 3 positively and 26 were doubtful. The Wassermann tests on all children showing doubtful reactions were repeatedly negative. The 3 children showing positive luetin reactions showed at no time any clinical evidence of lues, and gave negative Wassermann reactions. The Wassermann tests on the parents of these children were likewise negative. Among the children tested, 22.4 per cent gave a history of insanity in one or both parents, 10.8 per cent were illegitimate, 6.5 per cent were mentally backward, 35.8 per cent showed various pathological conditions. In spite of these circumstances, they all gave negative Wassermann reactions, a result which does not coincide with the reports of other workers. Contrary to the general opinion regarding the incidence of syphilis in child-caring institutions, the author's results must lead them to conclude that among the children of the Jewish poor of New York City syphilis is an exceedingly rare disease.

The Clinical Evaluation of the Wassermann Reaction.—Robert A. Kilduffe, Pittsburg. Archives of Dermatology and Syphilology, 1922, vol. vi, p. 147.

The clinical value of the Wassermann reaction is in direct proportion to the realization that it constitutes only a single method or phase of examination and that it should always be carefully correlated with and interpreted in the light of all other findings—however obtained—in the individual patient.

Studies of Syphilitic Serum Reactions.—K. Taoka, Tokyo. The Japan Medical World, 1922, vol. ii, p. 125.

The specific substance for Wassermann reaction in syphilitic serum is carried away with the flakes of Sachs-Georgi reaction in a certain ratio. By the removal of the flakes from the syphilitic serum, the remaining serum becomes negative to Wassermann and Sachs-Georgi reaction tests. The flakes of Sachs-Georgi reactions are dissolved by fresh serum or alkalin solution. The flakes of Sachs-Georgi reaction combine with complements. The ability of the flakes of Sachs-Georgi reaction to combine with complements is destroyed by a concentration above n/100 of alkalin or a concentration above n/100 of alkalin or n/400 of acid. The resistance of the flakes against the ions is the same as that of the syphilitic reactive substance of a serum. The flakes of Sachs-Georgi reaction can be divided into ether soluble and nonsoluble parts. When the antigen is added to the nonsoluble part it gives the specific Wassermann and Sachs-Georgi reactions. Thus it corresponds to the syphilitic reactive substance of the serum. As far as tested it did not give albumin reactions. The ether soluable part is composed of sufficiently active antigen. Each part, which was separated and became comparatively pure, can be recombined and gives the specific reaction. When the serum globulin is precipitated by 33 per cent of the saturation of ammonium sulphate solution, the syphilitic reactive substance is almost entirely removed into the precipitate. Only a part of it is removed with the globulin precipitated by the other methods. When a syphilitic serum is heated the Wassermann reaction is weakened, but Sachs-Georgi reaction, on the other hand, is strengthened. The Sachs-Georgi reaction is strengthened by the removal of a part of globulin of an unheated syphilitic serum. Globulin separated from an unheated serum either syphilitic or nonsyphilitic, has a strong anticomplemental action in the Wassermann reaction. This action of the globulin is destroyed by heating it before or after the separation. It is a thermolabile. The weakening of Wassermann reaction by heating a serum is not due to the destruction of the reactive substance, but due to the disappearance of the anticomplemental action of globulin. The Wassermann reaction with an unheated serum is liable to give a nonspecific positive reaction. An unheated globulin prevents the precipitation in the Sachs-Georgi reaction. This preventative action is disappeared by heating. It is a thermolabile. The reason an unheated serum does not give a precipitation reaction is due to this preventative action of globulin. The preventative action of unheated globulin differs with the complemental action of a serum. It seems to depend on the physicochemical action of globulin. Therefore a heated serum should be used in Wassermann and Sachs-Georgi reactions.

The Hecht-Weinberg-Gradwohl Test.—L. W. Famulener and Julia A. W. Hewitt, New York City. The Journal of Infectious Diseases, 1922, vol. xxxi, p. 285.

The authors found that the reactions with the Hecht-Weinberg-Gradwohl test were hardly so marked as with the Wassermann technic, but the Gradwohl modification might be considered somewhat superior when relying only on the results with the acetone-insoluble antigen in each method. On the other hand, the use of the cholesterinized antigen with the Wassermann method showed a stronger reaction with each positive serum (with one exception), and further gave a strongly positive reaction in one case—tertiary syphilis—which was negative with the Hecht-Weinberg-Gradwohl technic. In this report all serums giving positive reactions came from patients who gave a clear clinical history of syphilis, with the exception of one who had a suspicious history.

The Wassermann Reaction as an Index of Cure With Special Reference to the Value of Cold Fixation in the Technic of the Test.—C. H. Shearman, Australia. The Medical Journal of Australia, 1922, vol. i, p. 656.

The pathological processes attendant on a spirochaetal infection may result in unsuspected foci of infection remaining in spite of the most assiduous treatment. The methods of technic in vogue before the introduction of the ice-box technic are not sufficiently sensitive to indicate in the test result evidence of these clinically quiescent foci. A negative Wassermann test obtained by the older method of technic and sustained even for a considerable time after cessation of a prolonged course of treatment is therefore of doubtful value as an indication of cure. When the ice-box method of technic is used, indications of positivity are found to persist for a considerably longer period in the case of patients who have been treated than when the older method is used. The ice-box method, while being more sensitive, is very reliable and, if an approved technic be used, does not produce pseudopositive results in undiagnosed cases.

A Simple Quantitative Precipitation Reaction for Syphilis.—R. L. Kahn, Lansing, Mich. Archives of Dermatology and Syphilology, 1922, vol. v, p. 570.

In the author's opinion, this simple precipitation test should prove a valuable check on the Wassermann test. The importance of detecting syphilis is such that two tests should prove highly desirable. This disease is different from typhoid fever or diphtheria, for example. The patient does not recover from it in a sense that he recovers from the two other diseases. There are, indeed, those who believe that syphilis is not completely curable. May it not be possible that this belief has been evolved as a result of pronouncing syphilitic patients cured on the basis of apparent freedom from clinical symptoms and repeated negative Wassermann reactions, when in truth, lesions might still persist in a latent form? A test, therefore, which is more sensitive than the Wassermann, as the proposed precipitation reaction appears to be, should prove a valuable aid in the proper diagnosis of syphilis.

The Wassermann Test Performed With Chancre Fluid as an Aid to the Early Diagnosis of Syphilis.—Joseph V. Klauder, and John A. Kolmer, Philadelphia. Archives of Dermatology and Syphilology, 1922, vol. v, p. 566.

In employing this method, a fluid of unknown dilution is obtained. However, fluid obtained in this manner in one case yielded a four-plus reaction in 0.03 c.c., whereas the blood Wassermann reaction of the same patient collected at the same time and performed with the same technic yielded a negative reaction. A four-plus reaction in a high dilution of chancre fluid is not remarkable, in view of the fact that a similar reaction may be obtained with 0.001 c.c. of syphilitic blood serum. The authors have obtained a four-plus reaction in this dilution of serum in all stages of syphilis and uniformly in the untreated secondary stage. A positive reaction was obtained in the case of twelve of fourteen patients examined. Positive reactions were obtained from chancres which were treated locally as well as from those untreated; the dark-field was found negative as well as positive in the case group; secondary infection was absent in some cases and present in others. A clear uncontaminated fluid from the surface of the chancre is apparently not a requisite in obtaining a positive Wassermann reaction. It should be noted that conditions which cause the disappearance of spirochetes from the surface of the chancre and hence make the dark-field examination negative, local treatment with a spirocheticidal drug and pyogenic infection of its surface, apparently do not inhibit the local formation of the Wassermann fixing substances. Moreover, it is important to note that a positive Wassermann reaction with chancre fluid is obtainable before the reaction appears in the blood. This observation apparently excludes the hematogenous origin of the complement-fixing antibody and points to a local formation of these substances. Hence, there is apparently no objection to the presence of blood in the chancre fluid.

Studies in Asymptomatic Neurosyphilis.—Joseph Earle Moore, Baltimore. Bulletin of The Johns Hopkins Hospital, 1922, vol. xxxiii, p. 231.

It has been shown that early invasion of the central nervous system in syphilis is common, occurring in 26.4 per cent of a series of 352 patients with primary and secondary syphilis. Of 94 early neurosyphilitics, 72 were asymptomatic, and were detected only by the routine application of spinal puncture. Early asymptomatic neurosyphilis may be divided into three sub-groups on the basis of the spinal fluid findings and the response of the various groups to treatment. Invasion of the central nervous system probably occurs in the majority of all patients with syphilis, and unless the course of the disease is influenced from without (by treatment), this invasion takes place in most instances within the first year after infection. The ability of the invading organisms to produce clinical neurosyphilis probably depends on the defense mechanism of the individual patient. The experimental and clinical evidence bearing on these points are reviewed. Early asymptomatic neurosyphilis is more common in the white race than in negroes, but is equally frequent in men and women, of either or both races. Prolonged regular treatment influences favorably the incidence of early asymptomatic neurosyphilis. Irregular or lapsing treatment, on the other hand, markedly increases its incidence. A study of this material from the standpoint of strains of Treponema pallidum furnishes no support to the theory of the existence of a neurotropic strain of organism. That the spinal fluid abnormalities of early asymptomatic neurosyphilis are evidence of actual anatomical damage to the nervous system, is indicated by the frequency of certain minor subjective and objective neurologic signs, and of the significance of a persistently positive blood Wassermann reaction in treated patients, furnishes a clinical diagnostic aid for the recognition of neurologic invasion. Spinal puncture is an indispensable routine procedure in the management of early syphilis. Unless it is employed, many patients will be discharged as cured who are nevertheless candidates for clinical neurosyphilis. It should be performed as a routine after the first or second course of arsphenamine, and unless a lapse in treatment occurs, need not be repeated (if negative) until the end of treatment and the probation period. All three groups of asymptomatic neurosyphilis may be serologically and clinically ''cured'' by appropriate methods of treatment. Early asymptomatic neurosyphilis is the forerunner of clinical neurosyphilis.

A Plea for the Early Diagnosis and Treatment of Cerebrospinal Syphilis.—D. A. Gregory, Sioux Falls, S. D. The Journal-Lancet, 1922, vol. xlii, p. 90.

Neurosyphilis is, to a great extent, a preventable complication of syphilis. Early diagnosis and treatment of syphilis will lessen the incidence of neurosyphilis. Lumbar puncture gives more real information regarding the presence or absence of cerebrospinal syphilis than all other neurologic examinations. A cell count of over six, globulin increased with or without a positive Wassermann is, in a syphilitic, evidence of cerebrospinal involvement, even though other neurologic examinations are negative.

Observations on the Diagnosis of Neurosyphilis.—Irving H. Pardee, New York. New York Medical Journal and Medical Record, 1922, vol. cxv, p. 507.

The concurrence of visceral syphilis with neurosyphilis is appreciated by those of us who see many cases of the latter, but do we realize the frequency with which this occurs? The incidence as estimated in secondary syphilis is about twenty to thirty per cent and in tertiary syphilis from thirty-five up to fifty per cent. The author believes these early cases of neurosyphilis occurring as an accompaniment of secondary or early tertiary lues are the tabetics or paretics of a decade later. Spinal puncture is the one diagnostic procedure of greatest value in these cases. The serologic examination of the spinal fluid reveals things which are of importance in the diagnosis of neurosyphilis. An increased globulin, while not diagnostic, indicates inflammation within the subarachnoid space; a positive Wassermann reaction indicates the presence of syphilis, and is, of course, absolutely diagnostic, but the strength of the Wassermann test does not parallel the virulence of the neural infection, some cases of active neurosyphilis having a one-plus or a negative reaction.

The Status of Lumbar Puncture and the Prevention of its Complications.—Hugo W. Traub, Chicago. New York Medical Journal and Medical Record, 1922, vol. cxvi, p. 91.

It is submitted that so valuable a procedure as lumbar puncture should not be approached in a spirit of perfunctoriness; that it contains the elements of a minor surgical attack when properly safeguarded, though one with maximally awkward possibilities when indifferently executed; that most, if not all, of its dangers may be avoided by manometric control of the fluid, by the exercise of circumspection and the use of a certain amount of anatomical knowledge, and by the abandonment of its practice in the ambulatory patient altogether.

Diagnosis of Late Hereditary Syphilis and Lupus in Otorhinolaryngology.—Georges Portmann, Bordeaux, France. New York Medical Journal and Medical Record, 1922, vol. cxv, p. 508.

The diagnosis of late hereditary syphilis and of lupous tuberculosis is often extremely difficult, even with the help of the laboratory. Still it is essential to gather all the information that can be given by the laboratory, so as to obtain as much certainty as possible and not call too hastily scrofulate de vérole a lesion which is only syphilis or tuberculosis. Hybrid cases of syphilis and tuberculosis are most rare for out of 50,000 observations in the course of fifteen years (1900-1915) at the otorhinolaryngology department of the University of Bordeaux, only five cases are found to be diagnosticated scrofulate de vérole, without, besides, the assurance of the laboratory. But in four cases followed by the author since that time and which clinically seemed to be luposyphilitic hybrids, thorough laboratory researches have shown that one case was tuberculosis of a lupic form and the other three were cases which proved to be late hereditary syphilis.

Syphilis and Mental Deficiency: An Investigation of 217 Cases.—G. J. Key, Aberdeen and A. Pijper, Leyden, South Africa. South African Medical Record, 1922, vol. xx, p. 142.

In 217 cases of amentia the authors have, by means of the Wassermann reaction, demonstrated the presence of syphilis in 120, or 55.2 per cent. They have not been successful in observing any symptom, or group of symptoms, common to the cases giving a positive reaction. It is the authors' opinion that the syphilitic virus cannot be alone responsible for the amentia in all these cases. The chances are that some other predisposing cause is also present in most of them.

Syphilis as a Factor in Deafness.—C. H. McCaskey, Indianapolis, Indiana. The Journal of the Indiana State Medical Association, 1921, vol. xiv, p. 289.

Syphilis is much more frequently a causative factor than is supposed. Congenital or hereditary syphilitic deafness usually occurs early in life. Acquired luetic deafness is usually found in adult life. It attacks both the receptive and perceptive apparatus, but the latter much more frequently. It usually is bilateral in destruction of hearing. Diagnosis depends largely upon (a) case history, (b) laboratory findings, especially the Wassermann test, both blood and spinal fluid should be made. Bone conduction tests are of important value. Routine examinations of all cases by using all functional tests.

Is Syphilis Curable and Can it be Eradicated?—Victor G. Vecki, San Francisco. Archives of Dermatology and Syphilology, 1922, vol. vi, p. 318.

Neosilver arsphenamine is prompt in its action on primary symptoms. The induration disappears promptly; secondary skin lesions, papules and condylomata lata, which are generally very stubborn, invariably disappear after six or eight injections and one is always able to obtain a negative Wassermann reaction in from six to eight weeks, and by using a total of 3 to 6 gm. of the remedy. Late syphilis seems to be easier to influence whenever the Wassermann reaction is negative, although clinical symptoms allow no doubt about the diagnosis. It will take years of experience to learn about the duration of the Wassermann negative period, even though the blood be tested every month. The author has never seen any disagreeable by-effects from the use of neosilver arsphenamine. The author believes that the energetic, though cautious use of neosilver arsphenamine could not provoke albuminuria and cylindruria in originally intact kidneys. The statement that syphilis is a comparatively easily curable disease is no exaggeration; we may insist that all patients can be cured, but we must consider no case easy; in fact, we must approach each case as a rebellious one. It will be a great step toward the eradication of syphilis when the bulk of the medical profession becomes quite familiar with a character, and especially with the proper treatment, of syphilis. No doubt, we are progressing about rapidly. We must understand that syphilis is not a vice disease—just an infectious disease like any other. Again, we must give the patient the benefit of the doubt when he says he does not know, or when he tries to explain when and where he acquired the disease. Compulsory reporting of the disease to the health authorities would be a calamity—another slap at justice, another assault on the professional secret, and, while the mollycoddles may not care, another unconstitutional assault on personal liberty. When those in power will have been taught by the physicians of the country what syphilis does to humanity, then the city, state and national authorities will provide the necessary funds to fight the scourge. When the cost of insuring safety for every person, syphilitic or nonsyphilitic, is considered, also the cost of free, proper and kind treatment for the syphilitic person who cannot afford to pay his own way, it may be huge, but it still is quite insignificant when compared with the cost of maintenance of hospitals, asylums, prisons and orphanages populated by syphilitic persons and their tainted offspring, besides the amounts spent by persons who cannot afford it, in loss of time, medicine and treatment. In our country the depopulating influences of syphilis may not be of the same importance as in countries in which food for cannons must be raised, but the degenerating influence of the disease on the race is of more consequence. Progress in stamping out syphilis will be made when proper treatment shall be easy of access and easy to take, and when it will be made easy for every one to find out whether he has syphilis or not. We know that syphilis is a curable disease in the hands of an experienced syphilologist, but in order to abolish it antisyphilitic remedies must cease to be dangerous weapons in the hands of the majority employing them.

Observations on Ten Cases of Delayed Congenital Syphilis.—E. D. Spackman. The Lancet, London, 1922, vol. cciii, p. 65.

Syphilis hereditaris tarda is not a rare disease and should be diagnosed more frequently than it is in adult life. Aortitis or aneurysms may have a congenital origin and not be the result of acquired syphilis. All cases of syphilis, congenital or acquired, should be placed in the hands of those competent to treat them, and if any permanent benefit is to be expected such treatment must be intensive and thorough. Disease of the eye, in the form of interstitial keratitis, iritis, or choroiditis is often one of the earliest signs to appear, and is of great importance in early diagnosis.

Preliminary Report on Mercurosal.—Everette Erwin Butler, Louisville, Ky. The Therapeutic Gazette, 1922, vol. xlvi, p. 92.

Mercurosal is readily soluble in distilled water, .05 gram to 2 c.c. or .1 gram to 5 c.c. When administered intramuscularly it produces very slight, if any, pain at the site of the injection. When administered intravenously in the proper dosage and proper dilution, or even double that amount, no local or systemic reaction follows. No irritation or blocking of veins occurs, and the same vein may be used repeatedly for administration. Mercurialism is not at all likely when careful observation is kept of the patient. None of our patients showed any signs of mercurialism, even though we gave the maximum dose at frequent intervals. Mercurosal apparently yields the same therapeutic result as other active mercury preparations.

The Elimination of Arsenic in the Urine of Syphilitic Patients After Intravenous Injection of Arsphenamine.—Charles Weiss, Philadelphia. Archives of Internal Medicine, 1922, vol. 30, p. 85.

Only a small part of the arsenic derived from arsephenamine is eliminated by patients through the urine, 13.5 per cent being the highest amount in fourteen days. The largest amount of arsenic is eliminated in the first three days; after that uniformly small amounts are found in the urine. The elimination of arsenic is larger after the second and third doses are administered than after the first. Using constant doses of 0.7 gm. arsphenamine, there is considerable variation in the amounts of arsenic eliminated during a given interval of time by any one patient as well as by different patients presumably in the same stage of the disease and treated under the same conditions. The elimination of only small quantities of arsenic in the urine may be explained by the fact that a considerable quantity is eliminated through the feces and some is temporarily retained by the liver, kidneys, spleen, intestines and other parts of the body. A review of the literature on arsenic elimination and storage, and of the fate of the arsphenamine molecule in the animal body is given.

Spinal Drainage Following Intravenous Arsphenamine.—C. Burns Craig and L. Beverley Chaney, New York. The Journal of Nervous and Mental Disease, 1922, vol. 56, p. 97.

No single method of treatment is applicable to all cases. The intravenous administration of arsphenamine is the method of choice. Spinal drainage after intravenous administration of arsphenamine is not a hazardous procedure. Drainage will benefit some cases which have arrived at a position of inertia under intravenous administration alone. As satisfactory clinical and serological results may be obtained by intravenous arsphenamine and drainage as are produced by the intraspinous method and without the severe root-pains frequently set up by the latter method.

Neurorecurrences Following Treatment With Arsphenamine.—Ernest L. Zimmermann, Baltimore. Archives of Dermatology and Syphilology, 1922, vol. v, p. 723.

A series of thirty-nine neurorecurrences are tabulated. Their symptomatology, genesis and prognosis are discussed. Pathologically there are two types, a diffuse meningovascular process and a process limited to one or more focalized lesions. In the former the spinal fluid is always abnormal, in the latter it may show marked abnormalities or may be entirely normal. Prophylaxis of such lesions depends on a thorough mercurial treatment. It seems immaterial whether mercury is administered during or immediately following a course of arsphenamine.

Salvarsan-Jaundice: Its Causation, Incidence and Treatment.—Frederick Chamberlain, London. The Lancet, London, 1922, vol. ccii, p. 733.

Facts and figures are quoted. From these facts and figures certain conclusions are drawn. The author suggests treating the liver as though it were an old lady of strong Tory views, intolerant of changes and any deviation from the normal course of events. If the patient be a miserable specimen do not hesitate to use salvarsan, preferably supplemented by intramine. If none of the rules are broken it is improbable that jaundice will arise. If it does occur, take the patient into a hospital or nursing home, supplement the general treatment with intramine, used at one and in full doses.

Silver Arsphenamine in the Treatment of Syphilis.—J. Barrio de Medina, Madrid, Spain. Archives of Dermatology and Syphilology, 1922, vol. v, p. 321.

The author's opinion of silver arsphenamine is: silver arsphenamine is one more brand of arsphenamine which may be employed in the cases in which it seems to be indicated. It can be used only by specialists, because it has disadvantages which will prevent its general use, and it, therefore, must occupy a secondary place in the treatment of syphilis; at least, so far as the general practitioner is concerned.

The Technic of Arsenical Preparations in the Treatment of Syphilis.—John L. Laird, Philadelphia, Pa. The Therapeutic Gazette, 1922, vol. xlvi, p. 551.

Arsphenamine, neoarsphenamine and silver-arsphenamine are of value as antisyphilitic remedies in the order named. Silver-arsphenamine will be increased in efficiency if increased in dose. Concentration of arsphenamine solutions is to be avoided above 0.6 grm. of arsphenamine and silver-arsphenamine above 0.9 grm. and 0.25 grm. respectively to 50 c.c. of water. Dissolved oxygen in the water for solution is a most important factor toward toxic preparations of the arsphenamines.

The Standard of Cure in Syphilis.—A. Reith Fraser, Cape Town, South Africa. South African Medical Record, 1922, vol. xx, p. 102.

An adequate standard of cure must consider the following points:—A few spasmodic massive doses of arsenobenzene cannot be regarded as a serious effort to treat early syphilis. Wassermann readings, when their fallacies and limitations are fully appreciated, are of value in diagnosis. As a control of treatment or a guide to cure they are unreliable. Treatment directed against and controlled by the Wassermann reaction is misapplied. A slow and progressive sterilization should be preferred to a sterilization which is quick and sudden, and therefore probably incomplete. The drugs at our disposal should be employed in such a manner that their faculty of stimulating tissue defensive activity be utilized, in addition to their parasiticidal action. Such treatment should be continued for two or three years irrespective of Wassermann readings. Each case should be subjected to periodic clinical overhaul for the rest of his life. The necessity of this procedure should be impressed upon the patient at the time of his discharge from treatment. An adequately treated syphilitic may be permitted to marry at once. The wife of a syphilitic should be subjected to intensive treatment throughout the whole period of each succeeding pregnancy. The child should be treated from birth over a period of three years whether signs of the disease are present or not. The Wassermann reading in the newborn is not a reliable guide. A syphilitic woman may marry immediately adequate treatment is complete. She also must be subjected to treatment during each gestation, and her children treated from birth.

Observations on the Treatment of Syphilis in Pregnancy in the Department of Health in Detroit.—Walter E. Welz and Alfred E. Van Nest, Detroit Mich. The American Journal of Obstetrics and Gynecology, 1-22, vol. iv, p. 174.

Of the 147 syphilitic mothers cared for by the clinic, 46 had adequate treatment consisting of three or more injections of neosalvarsan and eight or more injections of mercury. These gave birth to 45 living children and one stillbirth, a fetal mortality of 2.1 per cent. The remaining 101 had insufficient or no treatment. These gave birth to 26 miscarriages or stillbirths with fetal development of from 16 to 40 weeks. This is a primary fetal mortality of 25.7 per cent for neglected cases. In this series were eight miscarriages at from 16 to 28 weeks. All of these were not treated. Of the 19 stillbirths occurring in the third period, 28 to 40 weeks, only one had full treatment and that was given in the third period of pregnancy. Five mothers who had full treatment in the first period (up to 16 weeks' pregnancy) gave birth to living children with no sign of syphilis. Nineteen mothers who had full treatment in the second period of pregnancy, 16-28 weeks, all gave birth to living babies. It was possible to obtain cord Wassermanns only from those babies born at Kiefer Hospital. Among these, some of the tubes were broken and the blood of others was anticomplementary. There were only 70 specimens which could be properly examined;—63 of these (78.7 per cent) were positive. Of the 79 cord Wassermanns examined 26 mothers had had full treatment. The result of the babies' Wassermann tests in these 26 cases was 8 (30 per cent) negative. From the 53 mothers who had no or insufficient treatment only 8 cord Wassermann tests were negative (15 per cent).

BOOK NOTICES

(Books for Review should be sent to Dr. W. H. Deaderick, Editor, Dugan-Stuart Bldg., Hot Springs, Arkansas.)

UNTERSUCHUNGEN ÜBER DEN SYPHILISERREGER.—By F. W. Oelze, Ph.D., M.D., Assistant in the Skin Clinic of the University of Leipsic. 74 pages, with 6 charts and 4 plates. Paper, 75 marks. Leipsic, Leopald Voss, 1922.

Certain attributes of the Spirocheta pallida have been carefully studied by Oelze. Among these are its spiral formation, the question of flagella, the relative advantages of Giemsa preparations examined by dark-field and transmitted light, the use of the color filter in the observation of Giemsa preparations by the light field, the use of polarized light with the clear field method, observation with the luminescent microscope of Lehman, the use of the ultramicroscope of Kohler with ultraviolet apparatus, individual measurements in stained preparations, measurements of organisms from primary and secondary syphilis and of nonpathogenic spirochetes, from the mouth, their locomotion, motion and false motion, the influence of solvents on spirochetes and the relation of therapy to the organism. Oelze concludes that examination of fresh preparations by means of the dark-field affords the most reliable results for diagnosis. This small work embodies the results of an enormous amount of laborious investigation and will doubtless prove of great interest and value.

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Original Articles

QUANTITATIVE STUDIES IN SYPHILIS FROM A CLINICAL AND BIOLOGICAL POINT OF VIEW

III. Arsenical Content in Scales, Blood and Urine in Arsenical and Nonarsenical Eruptions

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THE object of this communication is not to discuss arsphenamine or other drug eruptions but to make a preliminary report on the analysis of scales, blood and urine from patients who developed cutaneous manifestations after the use of the arsphenamine group as well as those from cases with analogous eruptions where the etiologic factor was unknown.

The types of response on the part of the skin to irritants of diverse nature often present the same clinical features, as witness urticarial rashes from irritants both from without and through the blood stream. For this reason we cannot always deduce the cause of an eruption from its objective appearance. In certain forms of exfoliative dermatitis where the etiologic factor is entirely unknown the clinical resemblance of such rashes so closely conforms to certain types of arsphenamine dermatitis that we have been led to suspect a possible arsenical causation and have been surprised in some of these cases to detect arsenic in the scales, the blood or the urine. Our researches up to this time have shown how widespread arsenic contamination is in drugs, in foods and in other articles which may be possible sources of intoxication. In addition to a dermatitis exfoliativa if symptoms of peripheral neuritis are also present, we have even stronger grounds to suspect this drug as an incriminating factor. Because of the well-recognized fact that arsenic by its action on the nerves produces herpes zoster one might infer that certain types of herpetiform eruptions which are followed by deep pigmentation might have a similar origin. In any event an investigation in certain cases along these lines is well worth while. Following the same line of reasoning we should investigate hyperkeratoses of the palms and soles in which other etiologic factors cannot be made to fit in with the clinical picture. Arsenic, as is well known, has a marked affinity for the epithelial cells and in chronic arsenic poisoning of a low grade it causes typical dyskeratosis, changes in the nuclei and cytoplasm of the cells together with marked hyperplasia resulting in warty growths and eventually epitheliomas. In widely disseminated eruptions of this character we see not infrequently all these changes—pigmentation, superficial scaling patches, keratoses, verrucous outgrowths and well marked squamous-celled epitheliomas—present in the same individual.

The problem of drug susceptibility applies less to arsenic perhaps than to other drugs which have a predilection for the skin. The percentage of patients who are oversensitive to arsenic medication is much less than occurs with the iodides or the bromides, for instance. The types vary from acute transient urticarial and erythematous eruptions to chronic forms of dermatitis exfoliativa involving in the latter case not only the skin but the mucous membranes as well. Individuals who possess this susceptibility may show it immediately or after the first few injections of arsphenamine. This complication is unfortunate for patients suffering from the early syphilitic infection as it limits our therapeutic measures to the less active drugs. If the initial cutaneous manifestations are disregarded or wrongly interpreted, further treatment may prove disastrous as shown by numerous reports in the literature. It is therefore important to instruct patients receiving arsenicals to report immediately to the attending physician any eruption on the skin. In the printed instructions given to our syphilitic patients at the Vanderbilt Clinic we emphasize the importance of examining their skin frequently after treatment. It has been noted in patients who are using mercury rubs and at the same time taking arsenic intravenously that a greater susceptibility to the effect of arsenic on the skin develops. In other words, the use of mercury externally may reduce the skin resistance to the arsenicals. A dermatitis resulting from the employment of sulphur in scabies might in an analogous way lower the skin resistance.

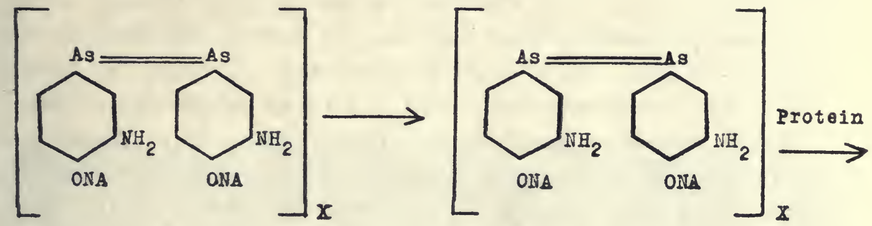
Patients with neurosyphilis with sensory disturbances of which pruritus is a marked symptom should also be carefully controlled and arsenicals administered with great care. To illustrate, we report the case of F. W., age thirty-five, weighing 120 pounds, with classical symptoms of an active tabes. On admission he complained of an intense generalized pruritus. He had never received arsenic in any form. Four injections of arsphenamine 0.3 gm. were administered intravenously at weekly intervals. He complained of an intensification of his itching after the first injections. Little attention was paid to this at the time but after the fourth treatment a generalized erythrodermia with edema of the face and extremities developed. Secondary pyodermia took place and the case terminated fatally. Had treatment been discontinued after the first or second injection such complication could have been averted. This accident occurred in the early days of the arsphenamine era before the accumulation of our present experience.

When arsphenamine is injected intravenously the solution is in the form of the disodium salt. The hydrogen-ion concentration of this solution is considerably above the normal value of the blood stream in which there is a large excess of hydroxyl ions. By means of natural processes there is a rapid adjustment in the equilibrium of the complex colloidal fluid and the normal value of $pH_{7.2}$ is again reached.

As this normal value is gradually reached a tendency toward precipitation takes place. In the previous interval the excess hydroxyl ion concentration has kept all of the elements in solution and allowed the chemical changes to take place in a gradual manner as obtained in an ideal dilute solution with ionic and molecular reactions catalysed by the presence of other salt-forming groups. In other words we are dealing with arsphenamine protein combination definite in character, which is soluble in excess of hydroxyl ions, precipitating at the neutral point, decomposing into more simple structures and finally eliminated either through the skin, urine, feces or breath. In some instances, a considerable amount of the drug is stored up in the tissues as illustrated in several of the cases of this group, showing delayed excretion. The probable mechanism of these changes is illustrated by the accompanying diagrammatic formula.

Phenolphthalein, procaine, orthoform and all types of drugs producing a dermatitis contain these phenolic groupings. Biochemically the deposition of either the arsenic or the phenolic groupings in the cutaneous layers is sufficient to produce irritation and resulting edema which prevent the functioning of the epidermis, the result being a parakeratosis with scale formation and desquamation.

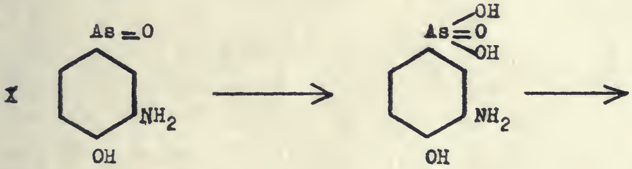
Careful observation of the tabulated results reveals the fact that analyses of the skin, blood, and urine present several instances in which the blood does not show determinable quantities of arsenic while the other two specimens contain it in considerable quantity. As pointed out in the previous papers the question of active and inactive arsenic has received serious thought. In other words there is a kinetic and a potential chemotherapy to constantly hold in mind and in explanation of this apparent anomaly two tentative principles seem to offer sufficient elucidation of this condition. In the first place one of us has demonstrated to our satisfaction that chemical combination takes place in the formation of precipitates accompanied by the usual pharmacodynamic phenomena. Deposition of the arsenic in the tissues later results, followed in some instances by a *gradual* elimination in a normal *manner* in contrast with an *intermittent* process accompanied by pathological symptoms and unusual manifestations. In this last case these suggestions find suitable application. The thought of falling objects observed through a single aperture gives a homely illustration of the condition. In only a few instances will the object be observed from this single aperture even though many objects are falling. The point from



Disodium arsphenamine solution as injected colloidal in physical structure. Trivalent form.

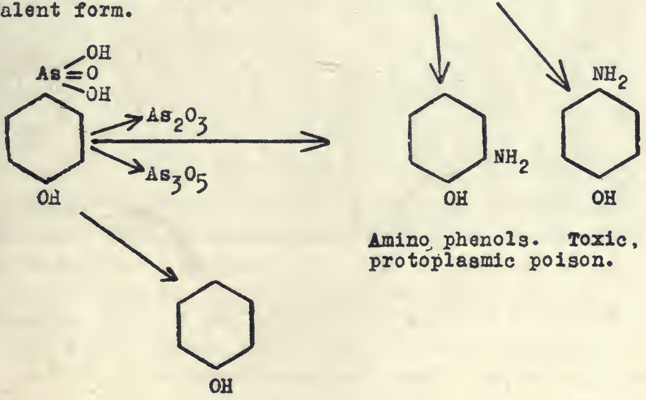
Disperse colloidal condition in blood stream. Trivalent form.

Protein Compound



Astive modification of arsenic preparation or nascent dynamic arsenic. Trivalent form.

2 amino 3 oxy Arsinic acid. Inactive.



Phenol arsinic acid

Amino phenols. Toxic, irritating protoplasmic poison.

Phenol

which the objects fall illustrates the skin or tissues from which the arsenic is derived. The blood is the aperture through which an occasional quantity of arsenic may be found. The urine is the place to which all the falling bodies descend. Through this means there is an intermittent elimination which may be detected at times.

In the second explanation it is well known that arsenic has power in some instances to produce pathological changes in the kidney, as well as in other tissues. This has been shown by work of Hooper at the U. S. Hygienic Laboratory. In this connection examination of the accompanying photomicrographs shows extensive necrosis of the uriniferous tubules some of which have been infiltrated with calcium salts (appears black in the photograph). The glomeruli appear quite normal in this particular section.

In the second section many of the uriniferous tubules in the cortex are entirely necrotic.

In the repair of the kidney these areas slough off and may carry with them large quantities of arsenic, and examination of the urine will show the presence of casts, albumin and other abnormal amounts of the products of excretion. There may also be a regeneration and repair of kidney tissue which may take place during the process of elimination of the arsenic. These products never again enter the circulation and offer a second plausible and reasonable explanation of the appearance of arsenic in the urine and none in the blood.

The following histories and appended charts tabulate the results of the analysis of the scales, blood and urine obtained from patients with arsenical rashes, a few nonarsenical eruptions having also been investigated for purposes of comparison.

CASE 1.—Serial Nos. 689 and 690. Diagnosis: Arsenical Dermatitis. A. F.; male; age thirty-two; latent syphilis. No history of primary sore; gonorrhea four years prior to admission to clinic. On examination enlarged epitrochlear and submental glands were found, otherwise no clinical evidence of syphilis; Wassermann 4+. From February 14, 1921, to July 27, 1921, he received 17 injections of arsphenamine 0.4 gm. each in two courses. About three weeks after the last he developed a dermatitis which covered the entire body, including the palms and soles.

His blood examined four weeks after the last injection contained no arsenic; his urine 0.095 mg. Two weeks later the urine showed 0.763 mg. and the blood 0.47 mg. (Serial Nos. 706 and 707).

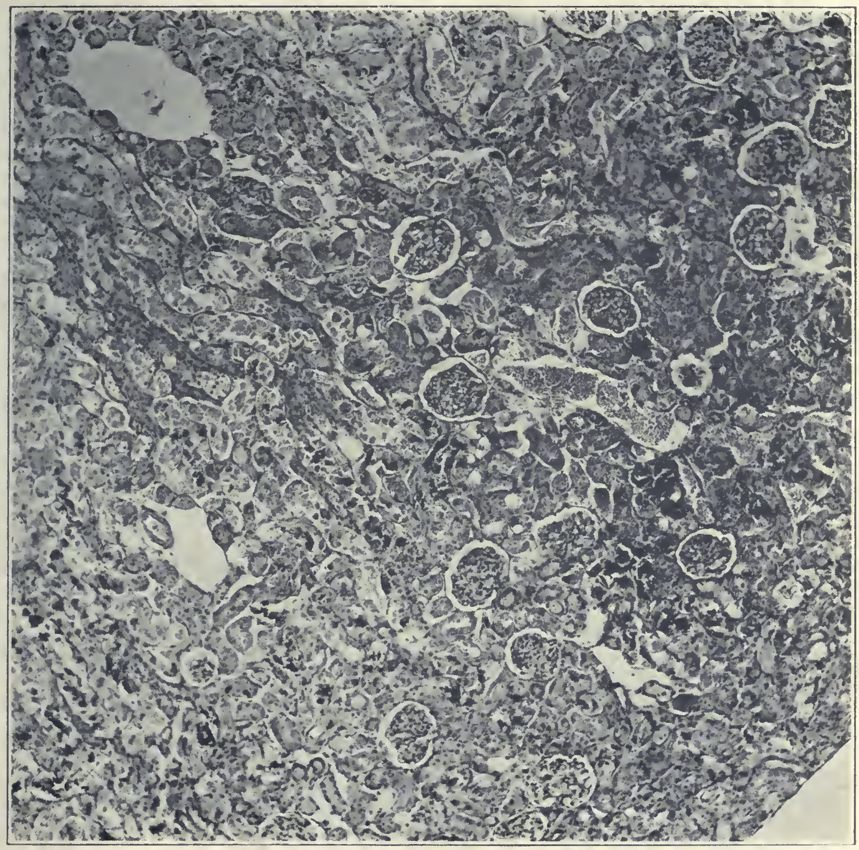


Fig. 1.—Kidney from rat given 150 mg. arsphenamine (disodium salt) per kilo, intravenously. Beef heart diet. Death on the second day. Kidney shows extensive necrosis of the uriniferous tubules some of which have been infiltrated with calcium salts (appears black in the photograph). The glomeruli appear quite normal. (Low dry lens magnification.)

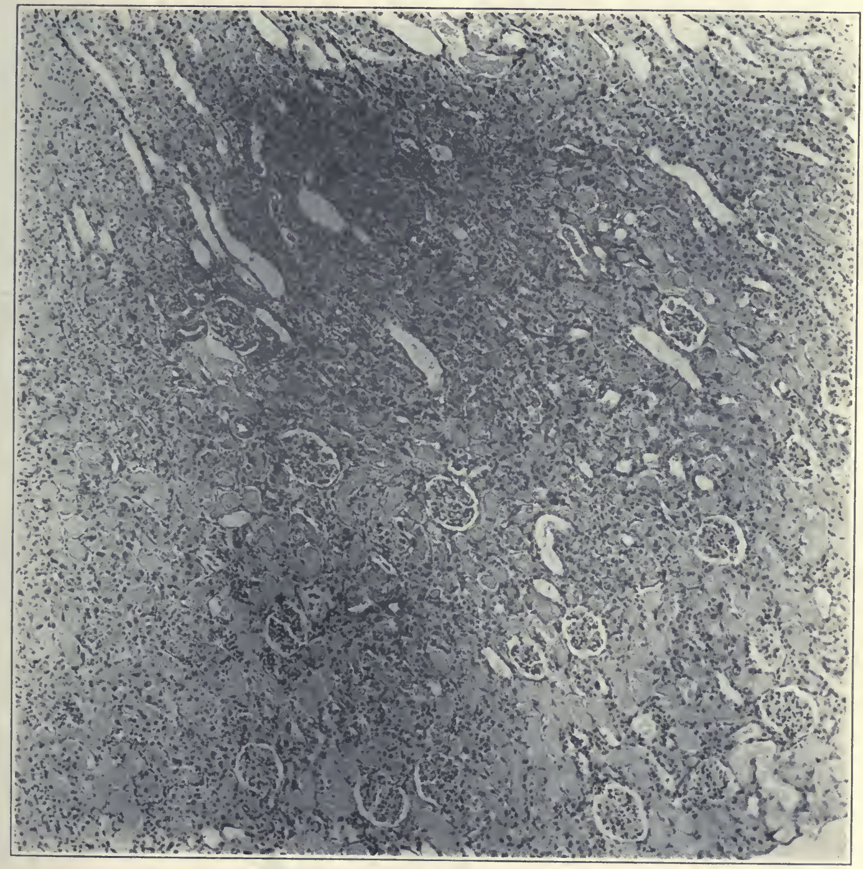


Fig. 2.—Kidney from rat given 150 mg. arsphenamine (disodium salt) per kilo, intravenously. Beef heart diet. Death on the second day. Many of the uriniferous tubules in the cortex are entirely necrotic. (Low dry lens magnification.)

We are indebted to Dr. C. W. Hooper of the H. A. Metz Laboratories, Inc., for the use of these sections.

Table I

PATIENT SERIAL NO.	DATE OF LAST INJEC.	NO. PREVIOUS INJECTIONS	DRUG USED	DOSE	TIME AFTER INJEC.	METHOD TREAT-MENT	WEIGHT OF SPECIMEN		PER-CENT SOLIDS	AS. IN MG. PER 100 GR. SPEC.	SP. GR.	AGE	SEX	DIAGNOSIS	LOCATION
							MOIST	DRY							
B. 957	12/5/21	6	S. Arsph.	0.125	7 days	I.V.	6.0961	1.4137	23.18	0.00		29	M	II. Syphilis Arsenical Dermatitis	Trunk and thighs.
U. 956							31.9452	1.0412	3.25	0.00	1.014				
B. 794	10/17/21	5	Arsph.	0.4		I.V.	3.1837	0.6710	21.07	0.074		44	M	Cerebrospinal Syphilis Arsenical Dermatitis	Palms.
U. 793							31.8830	1.9160	6.0	0.026	1.028				
S. 1429			Arsph.			I.V.		0.0190		315.9			F	Stomatitis, Edema and Desquamation involving the laryngo-pharynx. Dermatitis Exfoliativa (Arsenical)	Mucous membranes and entire body.
S. 1427						I.V.	4.3908			3.03					
S. 1428							0.6570			0.76					
B. 2337	10/2/22		13 Arsph. 22 S. Arsph. 14 Neoarsph.	0.3-0.45 0.15 0.45-0.6		I.V.	7.1270	1.6294	22.86	0.46		62	M	Neurosyphilis Arsenical Keratosis.	Palms.
S. 1431		6	Arsph.	0.4-0.6		I.V.		0.3976		1.9		55	M	Latent Syphilis Dermatitis Exfoliativa (Arsenical)	Entire body.
S. 1982		10	Arsph.	0.4		I.V.		2.7380		0.146		18	F	II. Syphilis Dermatitis Exfoliativa (Arsenical) Stomatitis	Body and Mucous Membrane.
B. 1383	3/1/22	4	Arsph.	0.3	36 hr.	I.V.	4.4218	0.9630	2173	0.103	1.022	24	M	III. Syphilis Arsenical Dermatitis	Entire body.
U. 1384							35.6495	1.6195	4.54	0.17					
B. 706	7/27/21	17	Arsph.	0.4	6 wk.	I.V.	6.5150	1.4025	21.52	0.47	1.022		M	Arsenical Dermatitis	Entire body.
U. 707							33.7850	0.9140	2.70	28.1					
B. 689	7/27/21	17	Arsph.	0.4	1 mo.	I.V.	7.3372	1.5286	20.83	0.00	1.023	32	M	III. Syphilis Arsenical Dermatitis	Entire body.
U. 690							35.3278	1.0339	2.90	0.095					
S. 1675								0.4825		4.14		51	M	III. Syphilis Dermatitis Exfoliativa (Arsenical)	Entire body.

TABLE I—CONTINUED

PATIENT SERIAL NO.	DATE OF LAST INJEC.	NO. PREVIOUS INJECTIONS	DRUG USED	DOSE	TIME AFTER INJEC.	METHOD TREATMENT	WEIGHT OF SPECIMEN		PER-CENT SOLIDS	AS. IN MG. PER 100 GR. SPEC.	SP. GR.	AGE	SEX	DIAGNOSIS	LOCATION
							MOIST	DRY							
S. 2319	10/16/22							4.4618		0.224				Dermatitis Exfoliativa (Arsenical)	Entire body.
B. 2017	8/23/22	12	Arsph.	0.4	3 wk.	I.V.	5.6664	1.2253	21.62	0.00		25	M	II. Syphilis Arsenical Dermatitis	Entire body.
U. 2016							26.1064	1.1753	4.50	0.5105					
S. 2072	9/13/22		Arsph.					1.1046		0.1499				Psoriasis	Generalized.
S. 2026	8/30/22		Arsph.			I.V.		0.1137		1.75				Dermatitis Exfoliativa (Arsenical)	Generalized.
S. 1859								3.8226		0.0130		45	F	Mycosis Fungoides	Generalized.
S. 2110		6	Arsph.	0.4		I.V.		2.4340		0.123		43	F	Latent Syphilis Dermatitis Exfoliativa (Arsenical)	Generalized.
S. 1433		6	Arsph. Neoarsph.	0.45		I.V.		0.1474		2.71		46	M	Latent Syphilis Dermatitis Exfoliativa (Arsenical)	Entire body.
S. 2306		6	Neoarsph.	0.9		I.V.		0.0809		9.88		18	F	II. Syphilis Dermatitis Exfoliativa (Arsenical)	Entire body.
S. 1498	1/6/22	4	Arsph.			I.V.		0.0192		5.208		26	F	III. Syphilis Dermatitis Exfoliativa (Arsenical)	Generalized.
S. 1499		6	Arsph.			I.V.		0.0808		1.23		50	M	Tabes Dermatitis Exfoliativa (Arsenical)	Generalized.
S. 2256								1.8680		2.14		61	M	III. Syphilis Dermatitis Exfoliativa (Arsenical)	Generalized.
B. 2257							9.9855	2.2246	22.27	0.00					
S. 2316	Sept. '22	8	Arsph.			I.V.		0.2977		0.00		66	M	III. Syphilis Arsenical Dermatitis	Entire body.
B_1. 2317							3.6213	0.2499	6.90	0.4001					
B_2. 2318							3.9800	1.2894	32.39	0.155					
U. 2382							33.8100	0.5409	1.59	0.369					

Table I—Continued

PATIENT SERIAL NO.	DATE OF LAST INJEC.	NO. PREVIOUS INJECTIONS	DRUG USED	DOSE	TIME AFTER INJEC.	METHOD TREATMENT	WEIGHT OF SPECIMEN		PER-CENT SOLIDS	AS. IN MG. PER 100 GR. SPEC.	SP. GR.	AGE	SEX	DIAGNOSIS	LOCATION
							MOIST	DRY							
S. 2320		4	Arsph.			I.V.		1.0572		0.00		58	M	Tabes Dermatitis Exfoliativa (Arsenical)	Generalized.
S. 2307		6	Neoarsph.			I.V.		3.8123		0.157		26	F	Latent Syphilis Arsenical Dermatitis	Generalized.
S. 1748						I.V.		1.0476		0.577		23	F	II. Syphilis	
S. 1647		4	Arsph.	0.3				0.0804		0.621				Dermatitis Exfoliativa (Arsenical)	Entire body.
B. 2308	8/30/22	2	Arsph.	0.3	3 wk.	I.V.	5.5627	1.1543	20.75	0.866		24	F	II. Syphilis Arsenical Dermatitis	Entire body.
B. 945	11/21/21	2	Arsph.	0.4	11 days	I.V.	4.6821	0.9950	21.25	Trace		46	M	Cerebrospinal Syphilis Arsenical Dermatitis	Entire body.
U. 944							31.0890	1.3884	4.46	0.00	1.012				
B. 1001					6 wk.		3.8795	0.9095	23.44	0.055					
U. 1000							30.7903	1.0081	3.27	0.59	1.020				
U. 1049					2 mo.		32.5550	0.6450	1.98	0.516	1.013				
B. 1050							3.9300	0.9725	24.74	7.500					
S. 2073			As_2O_3	1/20 grain		By mouth		1.2793		0.3572			F	Dermatitis Exfoliativa (Arsenical)	Generalized.
S. 1609		4	Arsph. 1 Neoarsph.	0.5 (?)		I.V.		0.0772		25.900		44	M	III. Syphilis Dermatitis Exfoliativa (Arsenical)	Entire body.
S. 1430			As_2O_3	1/30 grain 1/10 grain		By mouth		0.0610		1.630		30	F	Anemia Arsenical Keratosis	Palms and soles.
S. 1432								0.3200		56.20				Dermatitis Exfoliativa (Arsenical)	Entire body.
S. 2025								1.7197		Trace			F	Dermatitis Exfoliativa (Sq. Psoriasis)	Entire body.
S. 1724			Course of Na cacodylate 1 yr. ago.					1.8626		0.161			M	Mycosis Fungoides	Generalized.

Case 2.—Serial Nos. 793 and 794. Diagnosis: Arsenical Dermatitis. E. B.; male; age twenty-four; cerebrospinal syphilis. From August, 1921, to February, 1922, he was given 15 injections of arsphenamine 0.4 gm. each in two courses. After the fifth injection he developed an erythematous eruption on both hands which on account of the limited area was not suspected at the time of being due to arsenic. The treatment was continued without aggravation or spreading of the eruption; the lesions, however, persist at the original sites. His urine examined after the 5th injection showed 0.026 mg. and his blood 0.074 mg. of arsenic.

Case 3.—Serial Nos. 944 and 945. Diagnosis: Arsenical Dermatitis. A. S.; male; age forty-six; weight 160 pounds; cerebrospinal syphilis. Primary lesion twenty-two years ago for which he had inunctions only. When he came to the clinic he had symptoms referable to involvement of the central nervous system, a strongly positive Wassermann reaction in the blood and a strongly positive spinal fluid with a paretic curve. He was given an injection of arsphenamine 0.4 gm. and 12 to 14 hours later developed an erythematous eruption associated with chills, temperature and edema of the face and eyelids; the pruritus was intense. After two or three weeks the erythema and edema subsided leaving the skin pigmented. Following rest periods both neoarsphenamine and silver arsphenamine were tried, each time with the same experience. We thereupon decided not to treat him further with the arsenicals whereat he left our clinic and placed himself under the care of another institution without telling the physician in charge of his susceptibility. He was here given an injection of arsphenamine and reacted in the same manner as before.

Urine obtained 11 days after his second injection contained no arsenic; his blood a trace. Six weeks after (Serial Nos. 1000 and 1001) the urine showed 0.59 mg. and the blood 0.055 mg. Two months after (Serial Nos. 1049 and 1050) his urine showed 7.5 mg. and his blood 0.516 mg. arsenic.

Case 4.—Serial Nos. 956 and 957. Diagnosis: Arsenical Dermatitis. W. B.; male; age twenty-nine; secondary syphilis. He received 6 injections of silver arsphenamine 0.125 gm. at weekly intervals. Two or three days after the last one he developed a papulo-vesicular eruption limited to the trunk and thighs resembling dermatitis herpetiformis. His blood and urine examined one week after the last injection were free from arsenic.

Case 5.—Serial Nos. 1383 and 1384. Diagnosis: Arsenical Dermatitis I. D.; male, age twenty-four; weighing 142 pounds, came to the clinic with a syphiloderm of the trunk and left hip; no history of primary lesion. He was given 4 injections of arsphenamine 0.3 gm. at weekly intervals. Thirty-six hours after the last one he developed a generalized scarlatiniform eruption with vomiting and a temperature. He was obliged to remain in bed for several days until the acute symptoms subsided; when he reported again, a distinct finely desquamating eruption was present from head to foot. Under the use of bland ointments and lotions it disappeared after four to five weeks. His blood and urine examined five days after the last injection contained 0.103 and 0.17 mg., respectively.

Case 6.—Serial Nos. 1427 and 1428. Diagnosis: Dermatitis Exfoliativa (Arsenical). Two different lots of scales were examined from this patient whose skin eruption followed the use of arsphenamine. The first contained 3.03 mg. and the second lot sent at a later period 0.76 mg. arsenic.

Case 7.—Serial No. 1429. Diagnosis: Dermatitis Exfoliativa (Arsenical). This patient had been given intensive mercurial treatment from which she developed a marked stomatitis, edema and desquamation involving the laryngopharynx. This probably predisposed her to the action of arsenic for the use of arsphenamine was followed by an exfoliating dermatitis, the scales of which contained 315.9 mg. of the metal. The case terminated fatally shortly after from an influenza pneumonia.

Case 8.—Serial No. 1430. Diagnosis: Arsenical Keratosis of the Palms and Soles. Mrs. T., age thirty, was treated for anemia with arsenous acid, gr. 1/30 t. i. d. for a month and then gr. 1/10 t. i. d. for an indefinite period. About one month after the use of the latter dose, palmar and planter surfaces became rough and scaly and gradually the skin became very much thickened. The scales examined in this case were obtained after the eruption had been present a year and showed 1.630 mg. arsenic.

Case 9.—Serial No. 1431. Diagnosis: Dermatitis Exfoliativa (Arsenical). The patient was a man, fifty-five years old, who admitted a chancre thirty years previously for which he had had many courses of mercury inunctions and several courses of arsphenamine. The treatment immediately preceding his rash consisted of inunctions and 6 intravenous injections of arsphenamine 0.4 and 0.6 gm. at weekly intervals. His scales yielded 1.9 mg. arsenic.

Case 10.—Serial No. 1432. Diagnosis: Dermatitis Exfoliativa (Arsenical). These scales from a case of universal exfoliating dermatitis following arsphenamine contained 56.2 mg. of arsenic.

Case 11.—Serial No. 1433. Diagnosis: Dermatitis Exfoliativa (Arsenical). B. L.; male; age forty-six; was infected with syphilis fifteen years ago and treated with protoiodide pills for eleven years. He was then put on intermittent mercury and arsphenamine therapy. After the third injection of the latter he developed a violent generalized dermatitis and jaundice. He was again treated persistently with mercury alone. He then consulted another physician who advised neoarsphenamine. After the second injection of 0.45 gm. he developed a severe dermatitis exfoliativa from the scales of which 2.71 mg. of arsenic were obtained.

Case 12.—Serial No. 1498. Diagnosis: Dermatitis Exfoliativa (Arsenical). These scales came from a patient, age twenty-six, who was treated with arsphenamine because her child had an interstitial keratitis. After the third injection given December 24, 1921 she became nauseated, vomited and had dizzy spells; this was followed by a generalized scarlatiniform eruption. Making a good recovery she was again treated on January 6, 1922. Shortly after, an intense erythema with subsequent exfoliation appeared. Analysis of these scales yielded 5.208 mg. of arsenic.

CASE 13.—Serial No. 1499. Diagnosis: Dermatitis Exfoliativa (Arsenical). A man, aged fifty, suffering from advanced tabes, received 6 injections of mercury and 6 injections of arsphenamine. This was followed by an erythema with subsequent desquamation. The scales at the height of the disease showed 1.23 mg. of arsenic.

CASE 14.—Serial No. 1609. Diagnosis: Dermatitis Exfoliativa (Arsenical). The patient was a man, forty-four years old, who had received 4 injections of arsphenamine two years previously. After each one he suffered from a dermatitis with considerable desquamation. The present attack was said to follow an injection of 0.05 gm. silver arsphenamine. These scales yielded 25.9 mg. of arsenic.

CASE 15.—Serial Nos. 1647 and 1748. Diagnosis: Dermatitis Exfoliativa (Arsenical). This patient was a young woman 4 months pregnant, in the secondary stage of syphilis, who was given 4 intravenous injections of arsphenamine 0.3 gm. at weekly intervals. After the last one she had a very severe reaction, miscarried and developed an exfoliating dermatitis. From the first batch of scales 0.621 mg. of arsenic were obtained, and from a lot taken three weeks later 0.577 mg.

CASE 16.—Serial No. 1675. Diagnosis: Dermatitis Exfoliativa. Mr. H., age fifty-one, in the fall of 1921 had a vesicular rash on the backs of the forearms, in the axillae, the folds of the buttocks, the genitals, thighs and legs. Pruritus was very intense, preventing sleep and causing great nervousness. When seen in December, 1921, he had a scaling dermatitis over the extremities, the genitals, between the fingers and toes and on the lower part of his face. Bullae were present on the fingers. Several x-ray treatments and calamine and zinc lotion for the body were productive of temporary relief. When seen again three months later he had a universal exfoliative dermatitis with swelling of the face and eyelids. He complained of pruritus, pains and burning sensations. Bismuth subcarbonate and the sweet and bitter oils of almonds as well as an ointment containing zinc oxide were prescribed. Two months later furuncles appeared in the axillae and on the ankles, then deep-seated lesions with a red areola which on incision yielded a thick yellow pus and were undoubtedly metastatic. Several large abscesses also developed. He ran a temperature between 99 and 104 degrees. From his blood a pure culture of staphylococcus aureus was obtained. In about three weeks he succumbed to septicemia. Scales collected while the exfoliation was at its height yielded 4.14 mg. of arsenic. So far as could be learned this patient had not taken arsenic in any form. He had been on a very simple diet for months. He had, however, used over a long period calamine and zinc lotion and a zinc oxide ointment. As has been shown in a previous communication these preparations are contaminated with arsenic and its presence might be accounted for in this way.

Case 17.—Serial No. 1724. Diagnosis: Mycosis Fungoides. This patient was a man forty-two years of age with a negative family history. His present condition began about a year ago with the appearance of a psoriasis-like eruption on the trunk and extremities for which sodium cacodylate injections were given in one of the Out-Patient Departments. The rash did not disappear but changed in character and on admission to Mount Sinai Hospital he presented a generalized erythrodermia of a dusky almost violaceous hue interspersed with small tumors about the size of a hazelnut, especially on the extensor surfaces of the upper arms and sacral region. The blood examination varied from a normal picture to a high white count. Microscopical examination of the skin confirmed the diagnosis of mycosis fungoides. Analysis of the scales gave 0.161 mg. arsenic.

Case 18.—Serial No. 2110. Diagnosis: Dermatitis Exfoliativa (Arsenical). A woman, forty-three years old, received 6 injections of arsphenamine 0.4 gm. at weekly intervals. A rash appeared the second day after the last injection with universal exfoliation. These scales contained 0.123 mg.

Case 19.—Serial No. 1859. Diagnosis: Mycosis Fungoides. The patient, a woman forty-five years old, was in the Dermatological Service at Mount Sinai Hospital. Her history was negative for syphilis and tuberculosis. Excepting the diseases of childhood, she had been well until 7 years ago when an eruption appeared on the trunk and extremities for which she consulted her family physician. After several months it gradually disappeared. When seen at the hospital she had a generalized erythemato-squamous eruption, the lesions varying in size from a five cent piece to large plaques; they were salmon red in color, some distinctly infiltrated. The eruption had been present eight months. The clinical diagnosis of mycosis fungoides was confirmed by the microscope. Some thick greasy scales were removed and found to contain 0.0130 mg. of arsenic. As far as it was possible to determine she had had no internal medication containing this drug and the small quantity found might have had its source in the local applications she had received from her physician.

Case 20.—Serial No. 1982. Diagnosis: Dermatitis Exfoliativa (Arsenical). A young woman, age eighteen, with secondary syphilis, was reported to have had 32 grains of bichloride of mercury (bichloridol) in daily doses of one grain and 10 injections of arsphenamine and neoarsphenamine at weekly intervals. She developed a stomatitis, the entire mucous membrane from the oral opening to the anus apparently being involved before the skin rash appeared. Scales sent for examination contained 0.146 mg. of arsenic.

Case 21.—Serial Nos. 2016 and 2017. Diagnosis: Arsenical Dermatitis. H. K.; male; age twenty-five; secondary syphilitic rash. Twelve injections of arsphenamine, 0.4 gm. each, were administered over a period of three months. Three weeks after the last one a vesiculo-papular eruption appeared over the entire body. Owing to the associated edema and weeping the patient was admitted to Mount Sinai hospital and kept under observation. There was considerable puffiness and swelling of the eyelids and face, with edema of the ears and a moist papular eruption of the genital region. A temperature of 101° to 103.5° lasted for three weeks. At the height of the exanthem a large amount of albumin was present in the urine. Under a rigid diet and hospital care he gradually returned to normal. Three weeks after the last injection no arsenic was demonstrable in the blood and the urine showed 0.51 mg.

Case 22.—Serial No. 2025. Diagnosis: Dermatitis Exfoliativa following Psoriasis. These scales showed a trace of arsenic. It could not be learned whether the patient had taken this drug in any form.

Case 23.—Serial No. 2026. Diagnosis: Dermatitis Exfoliativa (Arsenical). This patient had received arsphenamine. Analysis of the scales yielded 1.75 mg. of arsenic.

Case 24.—Serial No. 2072. Diagnosis: Psoriasis. These scales from a patient taking arsenic for an extensive psoriasis contained 0.1499 mg. of the metal.

Case 25.—Serial No. 2073. Diagnosis: Dermatitis Exfoliativa. This patient was a woman with a generalized exfoliating eruption of two years' duration. So far as could be learned she had taken arsenious acid, gr. 1/20 t. i. d. for three weeks about 6 months previous to this examination. The scales contained 0.3572 mg. of arsenic.

Case 26.—Serial No. 2306. Diagnosis: Dermatitis Exfoliativa (Arsenical). The patient, eighteen years old, developed a desquamating eruption after the 6th injection of neoarsphenamine of 0.9 gm. The scales examined 7 weeks later contained 9.88 mg. of arsenic.

Case 27.—Serial No. 2307. Diagnosis: Dermatitis Exfoliativa (Arsenical). This patient, twenty-six years old, with latent syphilis, received 6 injections of neoarsphenamine, after which generalized exfoliation took place. Scales showed 0.157 mg. of arsenic.

Case 28.—Serial No. 2308. Diagnosis: Arsenical Dermatitis. A. S.; female; twenty-four years old; came to the Clinic on August 21, 1922, with a generalized erythematopapular syphilitic rash and condylomata about the vagina. On August 23 and August 30, 0.3 gm. of arsphenamine were administered. On the day following the second injection she developed a scarlatiniform dermatitis over the entire body with temperature and vomiting. The eruption was very pruritic and receded without scaling at the end of ten days. Her blood examined three weeks after the injection contained 0.866 mg. of arsenic.

Case 29.—Serial Nos. 2316, 2317, 2318, 2382. Diagnosis: Arsenical Dermatitis. C. O.; male; sixty-six years of age; had an initial lesion at the age of sixteen. He received no treatment and never had symptoms referable to syphilis. Four years ago in a routine examination it was found he had a four-plus Wassermann reaction. Protoiodide pills were prescribed and he took them for three years. In August, 1922, he suffered from a retinitis and a slight aortitis. In a European Clinic he was given 8 injections of arsphenamine over a period of two weeks. In September a dermatitis appeared which gradually involved the entire body except the face. About October 10, 1922 he developed partial suppression of the urine with albumin and casts. Scales collected the latter part of October were negative for arsenic; his blood showed 0.40 mg. and his urine 0.369 mg. of the metal.

CASE 30.—Serial No. 2319. Diagnosis: Dermatitis Exfoliativa (Arsenical). These scales from a patient who had been under arsphenamine therapy contained 0.224 mg. arsenic.

CASE 31.—Serial No. 2320. Diagnosis: Dermatitis Exfoliativa (Arsenical). The patient, a man fifty-eight years old with tabes was treated with one of the arsenicals. After the fourth injection he developed an erythema which after three weeks became exfoliative. No arsenic was found in the scales.

CASE 32.—Serial No. 2337. Diagnosis: Arsenical Keratosis of the Palms. E. C.; male; age sixty-two; neurosyphilis. From May 4, 1917 to January 5, 1921 he received 13 injections of arsphenamine 0.3 to 0.45 gm. and 14 injections of neoarsphenamine 0.45 to 0.6 gm. After each injection he had a severe reaction with chill. From January 25, 1921, to October 2, 1922, he received 22 injections of silver arsphenamine, the majority 0.15 gm. No reaction followed these. In the summer of 1922 he noticed a dryness and scaliness of his palms which condition gradually became more pronounced. His blood examined two weeks after the last injection showed 0.46 mg. of arsenic.

CASE 33.—Serial Nos. 2256 and 2257. Diagnosis: Dermatitis Exfoliativa (Arsenical). O. K.; male; sixty-one; history of syphilis twenty-five years previously. For ten years he had had a pruritic scaling eruption on right leg which was diagnosed and treated as eczema. In December, 1920, he received four weekly injections of arsphenamine for his syphilitic infection. Two weeks later he developed a generalized rash which became desquamating and continued until August, 1921. He remained free until June, 1922, when a similar attack occurred although he had received no arsenic in the meantime. Scales analyzed four months after onset showed 2.14 mg. of the metal; his blood was arsenic free.

SUMMARY

1. When normal elimination of arsenic through the skin is interfered with its deposition in the cutaneous layers is sufficient to produce irritation and consequent edema which prevents the functioning of the epidermis and results in an exfoliating dermatitis.

2. Fifty-one specimens of scales, blood and urine were examined; 22 batches of scales were from syphilitic patients who had developed a desquamating rash after the administration of the arsenicals; 20 of these were positive in amounts varying from 0.123 mg.

to 315.9 mg.; 2 were arsenic-free; 6 batches were from nonsyphilitic cases, the quantity fluctuating from a trace to 1.63 mg.; 3 of these patients were known to have received arsenious acid or cacodylate of soda. The presence of small amounts in the other 3 patients can be accounted for by diet or drugs applied externally.

3. Analysis of the blood and urine gave several instances in which the blood did not show determinable amounts of arsenic, while the urine contained it in considerable quantity.

The foregoing is only a preliminary report on the excretion of arsenic through the skin; at a later date we shall present a more comprehensive study.

The authors desire to acknowledge the generosity of Mr. H. A. Metz in contributing a part of the funds for carrying on these investigations.

They are also indebted to various physicians for furnishing specimens of scales for examination.

QUANTITATIVE STUDIES IN SYPHILIS FROM A CLINICAL AND BIOLOGICAL POINT OF VIEW

IV. Arsenic Content in the Blood at Various Intervals after Intravenous Injections of Salvarsan*

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THIS study is the first of a series of papers on the amount of arsenic in the blood, urine, and spinal fluid after injections of salvarsan, neosalvarsan, and silver-salvarsan. It is limited to an analysis of the blood after intravenous injection of salvarsan and resolves itself into the following questions:

1. When is the largest amount of arsenic found in the blood after such injections?
2. What amounts are found at varying intervals?
3. How long after the cessation of treatment can arsenic be detected in the blood?
4. Does the amount of arsenic found in the blood have any bearing on reactions and complications following treatment?

In a previous contribution on the normal arsenic content of the body fluids we have called attention to the fact that arsenic can be detected in the blood of individuals who have never received arsenic as such medicinally; its sources being dietary, occupational, drug contamination in preparations taken internally and used externally, and other unknown factors. In the consideration of the present problem, therefore, we shall have to bear these facts in mind as a possible explanation of apparent discrepancies. We made no attempt in these early studies to discover possible adventitious

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*I. The details of the method will be found in the first article, "Quantitative Studies in Syphilis from a Clinical and Biological Point of View," *American Journal of Medical Science,* clxiv, Oct., 1922, pp. 492-513.

II. "Normal Arsenic Content of the Body Fluid," in *Archives of Internal Medicine,* Vol. xxxi, 1923.

III. "Arsenical Content in Scales, Blood, and Urine, in Arsenical and Non-arsenical Eruptions," appears in this issue of the *American Journal of Syphilis,* p. 209.

sources, and have made our calculations on the known amount of the drug injected into the patient.

The analyses herewith were made on blood obtained from patients in the various stages of syphilis, and from a control group of non-syphilitic cases who had never had any treatment for this disease. The majority of the syphilitic patients were treated according to the method employed at the Vanderbilt Clinic, namely, two or more courses of eight intravenous injections of salvarsan by the gravity method at weekly intervals, unless they were in the primary or early secondary stages, when they were treated more intensively, that is, the first three injections every other day, and the remaining five at five and seven day intervals. Rest periods covered from four to twelve weeks. Old cases of neurosyphilis, after the third or fourth course, received injections at longer periods, namely, four, six, or eight weeks. Mercury salicylate was also given intramuscularly in courses of twelve to fifteen injections at weekly intervals. At no time was mercury given intravenously. Potassium iodide was administered to the latent and tertiary cases. It will be observed that many of the patients did not adhere to the plan outlined, but these are the usual difficulties met with in a large clinic.

The preparation of arsenic used was salvarsan from a batch, all the tubes of which bore the same control number.

On account of the large number of injections which are carried out in a single afternoon, it is necessary to use multiple doses of the drug in preparing the solution. In general, a 4 gram ampule is used as the unit for the preparation of the solution. The ampule is immersed in alcohol for several minutes before it is time to prepare the solution in order that any minute cracks in the glass may be detected and for the purpose of insuring great precaution in the use of the drug which might have undergone chemical change as a result of imperfection of the ampule.

To prepare the solution about 5 c.c. of cold, sterile, freshly distilled water for each decigram, at 20-22° C. is placed in a sterile Erlenmeyer flask. The ampule is opened and the contents slowly sprinkled on the surface of the water. The temperature is of great importance in its relation to the possibilities of forming products which are considerably more toxic. The drug should go into solution with little or no agitation within a few minutes. A slight amount of shaking may be resorted to. In every instance solution is greatly increased by avoiding the possibility of shaking with the ultimate formation of gummy masses which fail to be alkalinized at a later interval. When the salvarsan has *completely* dissolved, forming a perfectly clear solution with the absence of any gelatinous particles when viewed by transmitted light, it is ready for alkalinization. Correct alkalinization is an important factor and failure to alkalinize properly may be the cause of many table or immediate reactions. The alkali should be added all at once, using 0.84 c.c. of normal sodium hydroxide solution for each 0.1 gram of salvarsan. In the case of a 4 gram ampule 33.60 c.c. of a normal sodium hydroxide solution are required to form the disodium salt. This type of solution seems to be best tolerated by the patient. The solution is then filtered through previously moistened sterile gauze and diluted with cold, sterile 0.4 per cent sodium chloride, so that each decigram is dissolved in a final dilution of 20 c.c. The solution is then allowed to stand for ten or fifteen minutes before injection begins.

To reduce to a minimum contamination of the blood with extraneous arsenic, certain precautions were observed in taking specimens. The greatest possibility of error lay in the collecting of bloods immediately after treatment. To correct this the needle was retained in the lumen of the vein after the tubing of the gravity apparatus had been disconnected and a small quantity of blood permitted to flow out. Sterile salt solution was then poured over the needle and surrounding area to wash away this returned blood. Next, a sterile test tube was placed under the needle and the blood collected. For the later intervals the blood was drawn from the opposite arm. The needles used in obtaining these specimens were all sterilized separately from the treatment needles, to avoid arsenic contamination from the water in the sterilizer.

The average weight of the patients was about 60 kilograms, and the average dose of the drug was 0.4 gm. Blood volumes were not made in this series of analyses but it is generally accepted that there are about 85 c.c. of blood for each kilogram of body weight. On this basis there would be 5100 c.c. of blood for each patient. The average percentage solids in round figures was 22, giving 1122 gm. of total solids per patient. In 0.4 gm. of drug there are 126 mg. of metallic arsenic. If all of the arsenic remained in the blood stream there should be 11.2 mg. metallic arsenic per 100 gm. of dried specimen. As previously mentioned, the intravenous injection was carried out by gravity and the time required for the injection was about four minutes, or one minute for each decigram. By using needles of the same gauge and the same tubing each time this interval was kept very constant. With this idea in mind each interval is in reality a given time plus a varying interval from three to four minutes when the time of injection is considered.

It is well known that when arsenic is injected into the blood stream and is carried to all parts of the body, the amount deposited in the various tissues depends first, upon their vascularity, and secondly, upon their structure. The liver, for instance, being a very vascular organ and rich in cellular constituents, receives and stores larger amounts of arsenic than denser structures, such as connective tissue and muscle.

In the accompanying tables the relative rate of fixation of arsenic derived from the trivalent type of the drug has raised the question as to the site of fixation as well as the possibilities of localization. In the first article of this series several points of investigation were outlined, and in Articles II and III data are found which have a direct bearing upon the question of localized accumulation and its possible relation to certain types of intoxication occasionally observed, as post-arsphenamine manifestations, skin intoxications, jaundice, and other forms of intoxication from clinical observations. All these may occur with even a single injection or after repeated administration. These phenomena are readily explained on the basis of biological activity and the pharmacodynamic action of the drug as observed in the comparison of many individuals under different dietary conditions, other accompanying clinical complications, varying weights of the patient, frequency of treatment, which factors have an important bearing on the fixation determined by the organotropic action of this drug. The rate of oxidation of the organic arsenic protein precipitate and the rapidity of the change of the penetrability of the new product likewise influence the presence or absence of the drug in the body fluids. Recently it has been shown that a change in the ionic balance of the blood stream is an important factor in reducing the toxicity of the drug, also that the use of substances tending to affect a greater solubility of the drug will likewise have a bearing on the toxicity (sulphites, salt mixtures, carbohydrates, etc.). These phenomena obviously are in accord with the theories of chemotherapeutic action involving the principle of chemoreceptors of Ehrlich. It furnishes experimental evidence that parasites and tissue cells under certain *physical and chemical* conditions exert a varying affinity for the drug based upon principles of chemical reactivity in the presence of colloidal solutions as well as in the presence of neutral salts. Neutral salt (sodium chloride solution) has been used in the preparation of all our solutions. The relation of chemotherapy of organic arsenicals and their related physical-chemical phenomena together with its clinical application was first pointed out by us as an important factor. To what extent these factors influence the etiotropic action of the drug has not yet been determined. Kidney obstruction, impaired liver function (drug or syphilitic), and other visceral changes must ultimately be considered in the final analysis of our results. The influence of diuresis on excretion is an additional factor involved in the amount of arsenic that may be found in the blood stream at any one interval. The degree of arsenic saturation as the result of repeated and frequent intravenous medication has some bearing in determining the minimum threshold. These various points will be discussed from time to time in relation to the analysis of the other drugs used, as well as the excretion data at hand and the partition of arsenic between serum and clot.

The clinical aspect of these investigations will receive consideration on the completion of our studies with neosalvarsan and silver salvarsan.

(*Tables follow*)

TABLE I

Table I represents the detailed values obtained on blood at varying intervals after intravenous injection of salvarsan. In taking specimens for this table the timing was not made with an accuracy of 30 seconds. Total number of specimens 155.

BLOOD CHART I

SERIAL NO.	NO. PREV. INJEC.	DOSE OF DRUG	TIME AFTER INJEC.	WT. OF SPECIMEN		PERCENT SOLIDS	AS IN MG. PER 100 GMS. SPEC.	AGE	SEX	COLOR	DIAGNOSIS	WASS.
				MOIST	DRY							
779	2	0.3	Immed.	6.0570	1.1865	19.59	25.0	20	F	B	σIII	++++
819	5	0.4	“	6.2743	1.3065	20.82	1.70	?	?	?	Latentσ	++++
817	4	0.3	“	7.6900	1.5520	20.19	0.77	27	F	W	σII	++++
806	?	0.3	“	4.1935	0.7845	18.71	1.20	31	F	B	σIII	+
812	6	0.4	“	5.6090	1.1993	21.40	2.20	22	M	B	σIII	++++
1057	0	0.3	“	6.2913	1.3989	22.23	1.25	20	F	W	σII	++++
807	18	0.4	“	6.6080	1.2195	18.46	0.41	22	M	W	σII	+++
778	0	0.3	“	4.4570	0.8915	20.09	1.40	29	F	B	σIII	++++
811	9	0.4	“	7.2126	1.4597	20.24	27.5	?	?	?	Latentσ	++++
816	?	0.3	“	6.8551	1.3396	19.54	0.59	?	?	?	Latentσ	++++
1162	0	0.4	“	6.2977	1.4644	23.25	1.19	23	M	W	σII	++++
1026	14	0.4	“	6.9526	1.6370	23.54	0.61	31	M	W	σIII	+
1171	0	0.4	“	6.6038	1.5035	22.78	0.555	?	?	?	Latentσ	++++
782	0	0.4	“	6.3496	1.3636	21.48	9.1	28	M	W	σII	++++
805	20	0.4	“	6.7900	1.3008	19.16	0.61	32	F	W	σIII	++++
777	9	0.4	“	5.5350	1.1140	20.13	26.0	25	F	W	σIII	++++
822	0	0.3	“	6.6695	1.3605	20.40	0.85	34	F	W	σIII	++++
818	14	0.4	“	7.2356	1.5801	21.84	2.70	17	M	W	σIII	++++
1024	3	0.4	“	7.7860	1.7165	22.04	1.019	34	M	W	σII	++++
780	11	0.4	“	7.2700	1.4725	20.26	2.70	23	F	W	σIII	++
810	7	0.4	“	5.6225	1.2427	22.10	2.60	36	M	W	σIII	++++
1251	0	0.4	“	6.1901	1.2361	19.97	0.81	24	M	W	σIII	++++
786	4	0.3	“	5.6626	1.1146	19.70	1.10	32	F	W	σII	++++
783	4	0.3	“	8.4013	1.6744	19.93	2.90	21	F	B	σIII	+
1160	1	0.3	“	6.9913	1.4316	20.48	1.60	38	F	W	σIII	++++
821	3	0.2	“	4.9843	0.8026	16.10	0.62	22	F	B	σIII	++++
1163	5	0.4	“	5.3882	1.1634	21.59	0.25	27	M	W	σII	Neg.

830	10	0.3	Immed.	4.2887	0.7590	17.60	2.66	?	?	?	Latent σ	++++
879	7	0.4	10 min.	6.6965	1.3515	20.18	2.22	30	F	B	σIII	++++
545	6	0.3	“	7.1720	1.8439	25.70	0.434	25	F	W	σIII	++++
1330	0	0.4	“	6.5205	1.4835	22.90	0.339	37	M	W	σIII	++++
569	7	0.3	“	7.1950	1.4669	20.37	0.974	28	M	B	σIII	Neg.
885	18	0.4	“	3.1789	0.6379	20.06	0.41	23	F	W	σIII	++++
880	7	0.4	15 min.	5.8771	1.1795	20.06	0.84	30	F	B	σIII	++++
887	11	0.3	“	5.3495	1.1195	20.92	1.12	?	?	?	Latent σ	++++
58	4	0.4	20 min.	1.7620	7.1608	24.60	1.70	23	M	W	Cong.	++
45	0	0.3	“	6.3080	1.2540	19.87	0.479	38	F	W	σIII	+++
85	20	0.4	“	6.5990	1.4103	21.37	1.13	26	M	B	σIII	+
17	0	0.4	“	7.2025	1.6202	22.49	1.64	31	M	W	σIII	++++
11	0	0.4	“	9.6731	2.3254	24.11	1.03	26	M	B	σIII	++++
61	0	0.4	“	8.0442	1.7604	21.88	1.13	?	?	?	Nonsyph.	Neg.
14	0	0.4	“	6.7702	1.3610	20.12	0.734	27	M	W	σIII	++++
89	33	0.4	“	6.6716	1.4807	22.19	0.803	44	M	W	σIII	++++
51	5	0.4	“	7.1329	1.6560	23.19	2.41	40	M	W	σIII	Neg.
67	0	0.4	“	6.5016	1.4698	22.60	2.72	59	M	W	σIII	++++
828	7	0.4	“	4.7452	0.9205	10.40	0.271	19	F	B	σII	++++
99	16	0.4	“	7.4866	1.7850	23.84	0.980	39	M	W	σIII	++
52	0	0.4	“	5.1341	1.0923	21.30	1.80	32	M	B	σIII	++++
570	6	0.3	30 min.	1.7246	0.3874	22.46	1.30	25	F	W	σIII	++++
546	7	0.3	“	6.1466	1.5265	22.62	0.327	28	M	B	σIII	Neg.
886	18	0.4	“	6.8300	1.4626	21.41	1.36	23	F	W	σIII	++++
59	4	0.4	40 min.	7.7654	1.9264	24.80	0.311	23	M	W	Cong.	++
46	0	0.3	“	7.3011	1.5970	21.87	1.002	38	F	W	σIII	+++
86	20	0.4	“	4.4732	2.9637	21.56	0.310	26	M	B	σIII	+
18	0	0.4	“	8.5782	1.9800	23.08	1.01	31	M	W	σIII	++++
103	12	0.4	“	6.9396	1.7156	24.72	0.816	26	M	B	σIII	+
12	0	0.4	“	7.9380	1.7033	21.46	0.202	26	M	B	σIII	+++
62	0	0.4	“	8.9446	2.1694	24.25	1.53	?	?	?	Nonsyph.	Neg.
15	0	0.4	“	6.5515	1.2715	19.23	0.295	27	M	W	σIII	++++
90	33	0.4	“	7.6139	1.6366	21.49	1.95	44	M	W	σIII	++++
80	5	0.4	“	4.0572	0.9034	22.26	0.55	40	M	W	σIII	Neg.
871	26	0.4	“	4.6550	1.0700	22.98	0.70	40	F	W	σIII	++++
68	0	0.4	“	5.3230	1.2279	23.17	1.63	59	M	W	σIII	++++
53	0	0.4	“	9.8490	2.5090	25.37	1.95	32	M	B	σIII	++++

Blood Chart I—Continued

SERIAL NO.	NO. PREV. INJEC.	DOSE OF DRUG	TIME AFTER INJEC.	WT. OF SPECIMEN MOIST	WT. OF SPECIMEN DRY	PERCENT SOLIDS	AS IN MG. PER 100 GMS. SPEC.	AGE	SEX	COLOR	DIAGNOSIS	WASS.
881	7	0.4	50 min.	4.8692	1.0062	20.66	3.21	30	F	B	σIII	++++
884	18	0.4	"	6.2470	1.3413	21.45	0.73	32	F	W	σIII	++++
867	1	0.3	"	4.6837	1.0186	21.74	1.63	36	F	W	σIII	++++
60	4	0.4	60 min.	6.3416	1.5286	24.10	0.2208	23	M	W	Cong.	++
47	0	0.3	"	5.1196	1.0386	20.28	1.92	38	F	W	σIII	+
790		0.4	"	5.4777	1.1260	20.55	3.10	38	M	W	σIII	++++
19	0	0.4	"	5.9900	1.4202	23.70	1.65	31	M	W	σIII	++++
13	0	0.4	"	8.4896	2.1550	25.38	0.14	26	M	B	σIII	++++
63		0.4	"	6.1436	1.4885	24.22	0.336	?	?	?	?	?
16	0	0.4	"	8.3216	1.6096	19.34	1.24	27	M	W	σIII	++++
91	33	0.4	"	7.3397	1.5783	21.50	0.374	44	M	W	σIII	++++
81	5	0.4	"	4.0572	0.9034	22.26	0.123	40	M	W	σIII	Neg.
69	0	0.4	"	7.4177	1.7125	23.08	0.584	59	M	W	σIII	++++
101	26	0.4	"	5.9460	1.4498	24.38	2.76	39	M	W	σIII	++
54	0	0.4	"	7.7222	1.6332	21.15	0.368	32	M	B	σIII	++++
597	0	0.4	24 hr.	4.8240	1.0475	21.71	0.047	24	M	B	σII	++++
543	0	0.4	"	5.4030	1.2396	22.75	0	19	M	W	σII	Neg.
539	0	0.3	"	6.8214	1.5888	23.29	0.0315	37	M	B	Nonsyph.	Neg.
541	0	0.3	"	6.5391	1.2941	19.80	0.232	35	F	B	Nonsyph.	Neg.
591	6	0.4	"	5.0796	1.2257	21.58	0.326	27	M	W	Latentσ	Neg.
595	2	0.4	"	5.4546	1.3046	23.91	0.306	40	M	W	σIII	+++
565		0.3	"	6.8394	1.6110	25.01	0.062	?	?	?	Latent	?
564	0	0.4	"	5.8891	1.2179	20.68	0.205	34	M	W	Nonsyph.	Neg.
593	0	0.4	"	7.4562	1.7731	23.78	0	?	?	?	Latent	?
20	2	0.4	"	8.6254	2.0581	23.86	0.240	22	F	B	Nonsyph.	+
1236	0	0.3	"	7.3565	1.6753	22.76	Trace	34	M	W	Nonsyph.	Neg.
1126	0	0.5	"	6.4708	1.3602	21.02	0.14	?	?	?	Latent	?
568	0	0.3	"	6.1229	1.3580	22.17	1.37	?	?	?	Nonsyph.	Neg.
1329	0	0.3	"	6.1400	1.3850	22.57	0.97	26	M	B	Nonsyph.	Neg.
514	0	0.3	"	7.5331	1.7206	22.84	0.029	32	M	B	Nonsyph.	Neg.
596		0.3	"	8.0422	1.6968	21.09	0.029	37	F	W	σIII	Neg.

540	0	0.4	48 hr.	7.0451	1.7133	24.31	Trace	37	M	B	Nonsyph.	Neg.
550	0	0.4	“	5.8422	1.4731	25.59	0.034	29	M	B	Nonsyph.	Neg.
542	0	0.4	“	4.3774	0.8864	20.24	0.113	35	F	B	Nonsyph.	Neg.
592	0	0.4	“	5.0428	1.1003	21.81	0.708	21	M	W	σII	Neg.
567	0	0.4	“	8.9410	1.9892	22.24	0.050	?	?	?	Latentσ	++++
1058	0	0.3	“	6.8771	1.5786	22.95	0.253	20	F	W	σII	++++
1161	1	0.3	“	5.8192	1.3764	23.65	1.03	20	F	W	σII	++++
598	0	0.3	“	5.3664	1.1462	21.35	0.0872	28	F	B	Nonsyph.	Neg.
1237	0	0.2	“	6.8712	1.6636	24.21	0.030	34	M	W	Nonsyph.	Neg.
1125	0	0.5	“	6.3150	1.3895	22.003	0.108	?	?	?	σLatent	++++
566	0	0.3	“	6.5830	1.3768	20.89	0.72	?	?	?	Nonsyph.	Neg.
515	0	0.3	“	7.5323	1.8638	24.75	Trace	32	M	B	Nonsyph.	Neg.
594	0	0.4	“	6.5956	1.6691	25.33	0.359	?	?	?	Nonsyph.	Neg.
1238	0	0.2	72 hr.	4.0600	0.9603	23.65	0.052	34	M	W	Nonsyph.	Neg.
1102	0	0.5	“	4.7600	1.0430	21.91	0.289	?	?	?	Latentσ	++++
895	11	0.2	4 day	4.1344	0.8055	19.48	1.6	6	F	W	Cong.	++++
1054	0	0.4	“	7.1252	1.6602	23.30	Trace	33	M	B	σII	++++
1066	4	0.3	5 day	6.8537	0.9137	20.21	0.548	21	F	W	σII	++++
1234	1	0.4	1 wk.	6.3250	1.6057	25.38	0.124	?	?	?	Latentσ	++++
87	30	0.4	“	5.9444	1.2352	20.777	3.88	28	F	W	σII	Neg.
105	3	0.3	“	8.1782	1.5805	19.327	0.633	22	F	B	σIII	++++
106	38	0.4	“	6.6680	1.6260	24.237	1.23	40	M	W	σIII	++
88	2	0.3	“	6.8856	1.5306	22.237	4.35	24	F	B	σIII	+++
104	8	0.3	“	6.9679	1.4014	20.117	0.35	?	?	?	Latent	++
220	9	0.4	“	6.4374	1.5350	23.84	0.489	32	M	B	σIII	++++
1098	1	0.3	“	8.8162	2.1360	24.20	0.023	22	F	W	σII	?
70	8	0.4	“	2.4438	0.5527	22.617	0.905	?	?	?	Latentσ	++++
114	9	0.4	“	7.4188	1.5170	20.44	2.30	43	M	W	σIII	++++
110	14	0.4	“	8.7123	2.3212	26.63	3.89	40	M	W	σI	Neg.
1164	1	0.4	“	5.7958	1.2882	22.23	0	32	M	B	σIII	++++
108	7	0.2	“	6.8430	1.3248	19.35	1.76	22	F	B	σIII	++++
57	23	0.4	“	6.2701	1.3831	22.057	2.17	25	M	W	σIII	++++
832	18	0.2	“	2.2559	0.4573	20.27	7.2	7	F	W	Cong.	++++
862	17	0.15	“	1.8471	0.3636	19.68	0.27	5	M	W	Cong.	++++
858	18	0.15	“	4.0841	0.8916	21.83	17.0	4	M	W	Cong.	++++
860	19	0.2	“	2.9745	0.6060	20.37	0	2	F	W	Cong.	++++

BLOOD CHART I—Continued

SERIAL NO.	NO. PREV. INJEC.	DOSE OF DRUG	TIME AFTER INJEC.	WT. OF SPECIMEN MOIST	DRY	PERCENT SOLIDS	AS IN MG. PER 100 GMS. SPEC.	AGE	SEX	COLOR	DIAGNOSIS	WASS.
56	19	0.4	1 wk.	10.0510	2.2360	22.25	0.112	25	M	B	σIII	Neg.
1059	7	0.4	"	6.7184	1.6059	23.90	1.2	?	?	?	Latent	++
22	5	0.4	"	7.8222	1.6672	21.31	1.19	35	F	B	σIII	++++
71	3	0.4	"	6.3126	1.6283	25.63	0.859	?	?	?	Latentσ	++++
72	4	0.4	"	10.2231	2.6010	25.44	0.512	30	M	B	σIII	++++
1281	1	0.4	"	6.6700	1.3800	20.70	0.1089	42	M	B	σIII	++++
1064	0	0.4	"	6.1783	1.4797	23.95	0.603	18	F	W	σIII	++++
107	2	0.3	"	6.9874	1.4511	20.76	0.603	49	F	W	σIII	++++
1174	7	0.4	9 day	5.1884	1.2054	23.23	2.6	?	?	?	Latent	++
949	7	0.4	6 wk.	6.2034	1.3418	21.64	0.037	?	?	?	Latent	++
982	5	0.3	"	4.8046	0.9275	19.30	0.32	21	F	B	σIII	+
928	23	0.4	2 mo.	4.1535	1.0068	24.83	1.6	36	M	W	σIII	++++
1073	7	0.4	"	8.3121	1.8055	21.72	0.1108	?	?	?	Latentσ	++++
924	8	0.4	"	4.8525	1.1449	23.60	Trace	41	M	W	σIII	++++
1158	23	0.4	"	6.4821	1.5915	24.54	0.12	34	M	W	σII	++++
1104	7	0.4	"	9.4882	2.1802	23.00	Trace	?	?	?	Latentσ	++++
1152	13	0.4	3½ mo.	5.2645	1.2389	23.53	0	27	M	W	σII	Neg.
1048	7	0.4	6 mo.	4.7738	1.1488	24.06	Trace	29	M	B	σIII	++++
1023	19	0.4	8 mo.	......	1.6126	.....	0.12	40	M	W	σIII	++++
947	7	0.4	10 mo.	7.7810	1.6335	20.99	0	23	M	W	Cong.	++
926	8	0.4	1 yr.	5.0060	1.1107	21.98	1.69	25	M	W	σIII	Neg.
965		0.4	"	7.1934	1.6285	22.65	0.307	28	F	W	σIII	Neg.
995	9	0.4	1½ yr.	4.1521	0.9876	23.78	0.202	47	M	W	σII	Neg.
1275	0	0.4	3 yr.	8.1590	1.6604	20.35	0.18	32	M	B	σIII	++++

Detailed Analyses of Tables I and II, Giving the Number of Cases in the Group with the Wassermann, Dose of Drug, and Number of Previous Injections Together with the Highest Arsenic Value, the Lowest Arsenic Value, and the Average Amount Found in This Group.

INTERVAL—IMMEDIATE

SECONDARY SYPHILIS: 8 cases; Wassermann positive.
No. of previous injections: 0–18.
Dose: 0.3 gm.; 3 cases; 0.4 gm.; 5 cases.
Smallest amount of arsenic: 0.25 mg. after 0.4 gm.; 5 previous injections; male, white, aged 27.
Largest amount of arsenic: 9.10 mg. after 0.4 gm.; no previous injections; male, white, aged 28.
Average amount of arsenic: 1.88 mg.

TERTIARY SYPHILIS: 13 cases; Wassermann positive.
No. of previous injections: 0–20.
Dose: 0.2 gm., 1 case; 0.3 gm., 6 cases; 0.4 gm., 6 cases.
Smallest amount of arsenic: 0.61 mg. in 2 cases; one, male, white, aged 31, after 0.4 gm. and 14 previous injections; the other, female, white, aged 32, after 0.4 gm. and 20 injections, the last 16 days before.
Largest amount of arsenic: 2.90 mg. after 0.3 gm. and 4 previous injections; female, black, aged 21.
Average amount of arsenic: 1.60 mg.

LATENT SYPHILIS: 3 cases; Wassermann positive.
No. of previous injections: 0–10.
Dose: 0.3 gm., 1 case; 0.4 gm., 2 cases.
Smallest amount of arsenic: 0.555 mg. after 0.3 gm. and 12 previous injections, the last a month before; female, white, adult.
Largest amount of arsenic: 2.66 mg. after 0.3 gm. and 10 previous injections; adult, female, white.
Average amount of arsenic: 1.64 mg.

INTERVAL—10 MINUTES

TERTIARY SYPHILIS: 5 cases; 4 with positive Wassermann; 1 negative.
No. of previous injections: 1–18.
Dose: 0.3 gm., 3 cases; 0.4 gm., 2 cases.
Smallest amount of arsenic: 0.41 mg. after 0.4 gm. and 18 previous injections; female, white, aged 23.
Largest amount of arsenic: 2.22 mg. after 0.3 gm. and 7 previous injections; female, black, aged 30.
Average amount of arsenic: 0.886 mg.

(*Continued on p.* 244.)

TABLE II

Table II represents a detailed classification of the specimens found in Table I. These values are tabulated in respect to the stage of the disease and also in respect to the intervals at which the specimens were obtained and showing the arsenic content by groups.

BLOOD CHART II

SERIAL NO.	NO. PREV. INJEC.	DOSE OF DRUG	TIME AFTER INJEC.	WT. OF SPECIMEN		PERCENT SOLIDS	AS IN MG. PER 100 GMS. SPEC.	AGE	SEX	COLOR	DIAGNOSIS	WASS.
				MOIST	DRY							
						PRIMARY SYPHILIS						
						Interval—1 week						
110	14	0.4	1 wk.	8.7123	2.3212	26.64	3.89	40	M	W	σI	Neg.
						SECONDARY SYPHILIS						
						Interval—Immediate						
817	4	0.3	0 +	7.6900	1.5520	21.19	0.77	27	F	W	σII	++++
1057	0	0.3	"	6.2913	1.2989	22.23	1.25	20	F	W	σII	++++
807	18	0.4	"	6.6080	1.2195	18.46	0.41	22	M	W	σII	+++
1162	0	0.4	"	6.2977	1.4644	23.25	1.19	23	M	W	σII	++++
782	0	0.4	"	6.3496	1.3636	21.48	9.10	28	M	W	σII	++++
1024	3	0.4	"	7.7860	1.7165	22.04	1.019	34	M	W	σII	++++
786	4	0.3	"	5.6626	1.1146	19.70	1.10	32	F	W	σII	++++
1163	5	0.4	"	5.3882	1.1634	21.59	0.25	27	M	W	σII	++++
						Interval—20 minutes						
828	7	0.4	"	4.7452	0.9205	19.40	0.271	19	F	B	σII	++++
						Interval—24 hours						
597	0	0.4	24 hr.	4.8240	1.0475	21.71	0.0477	24	M	B	σII	++++
543	0	0.4	"	5.4030	1.2396	22.75	0	19	M	B	σII	Neg.
						Interval—48 hours						
1058	0	0.3	48 hr.	6.8771	1.5786	22.95	0.253	20	F	W	σII	++++
1161	1	0.3	"	5.8192	1.3764	23.65	1.03	20	F	W	σII	++++
						Interval—4 days						
1054	0	0.4	4 day	7.1252	1.6602	23.30	Trace	26	M	B	σII	++++

Interval—5 days												
1066	4	0.3	5 day	66.8537	0.9137	20.21	0.548	21	F	W	σII	++++
Interval—1 week												
87	30	0.4	1 wk.	5.9444	1.2353	20.777	3.88	28	F	W	σII	Neg.
1098	1	0.3	"	8.8162	2.1360	24.20	0.023	22	F	W	σII	++++
2632	5	0.4	"	3.3889	0.7075	20.87	2.12	25	M	W	σII	Neg.
Interval—10 days												
2645	3	0.4	10 day	3.9187	0.8863	22.61	2.82	23	M	W	σII	++++
2616	9	0.4	"	5.0031	1.1322	22.62	2.35	40	M	W	σII	++++
Interval—2 weeks												
2656	35	0.4	2 wk.	6.5613	1.4542	22.16	0.343	29	M	W	σII	++
2173	5	0.4	"	5.4746	1.3562	24.77	1.17	30	M	W	σII	++++
2652	18	0.4	"	3.3117	0.7168	21.64	1.11	25	M	W	σII	++++
Interval—3 weeks												
2157	26	0.4	3 wk.	5.0938	1.2487	24.51	0	29	M	W	σII	++
Interval—1 month												
2622	7	0.4	1 mo.	5.6000	1.2031	21.48	1.66	38	M	W	σII	++++
Interval—2 months												
1158	23	0.4	2 mo.	6.4821	1.5905	24.54	0.12	34	M	W	σII	++++
2171	5	0.4	"	3.9785	0.9147	23.24	0.218	23	M	B	σII	++
2639	13	0.4	"	5.3934	1.2339	22.89	0.810	23	M	W	σII	++++
Interval—2 years												
1021	4	0.4	2 yr.	4.8000	1.2814	26.69	0.15	32	M	W	σII	Neg.
TERTIARY SYPHILIS												
Interval—Immediate												
806	14	0.3	0 +	4.1935	0.7845	18.71	1.20	31	F	B	σIII	+
812	6	0.4	"	5.6090	1.993	21.40	2.20	22	M	B	σIII	++++
778	0	0.3	"	4.4370	0.8915	20.09	1.40	29	F	B	σIII	++++

Blood Chart II—Continued

SERIAL NO.	NO. PREV. INJEC.	DOSE OF DRUG	TIME AFTER INJEC.	WT. OF SPECIMEN		PERCENT SOLIDS	AS IN MG. PER 100 GMS. SPEC.	AGE	SEX	COLOR	DIAGNOSIS	WASS.
				MOIST	DRY							
				Tertiary Syphilis—Continued								
				Interval—Immediate—Continued								
1026	14	0.4	0 +	6.9526	1.6370	23.54	0.61	31	M	W	σIII	+
805	20	0.4	"	6.7900	1.3008	19.16	0.61	32	F	W	σIII	++++
822	0	0.3	"	6.6695	1.3605	20.40	0.85	34	F	B	σIII	++++
818	14	0.4	"	7.2356	1.5801	21.84	2.70	17	M	W	σIII	++++
816	?	0.3	"	6.8551	1.3396	19.54	0.59	?	?	?	Latentσ	++++
780	11	0.4	"	7.2700	1.4725	20.26	2.70	23	F	W	σIII	++
777	9	0.4	"	5.5350	1.1110	20.13	26.00	25	F	W	σIII	++++
810	7	0.4	"	5.6225	1.2427	22.10	2.60	36	M	W	σIII	++++
811	9	0.4	"	7.2126	1.4597	20.24	27.50	?	?	?	Latentσ	++++
1251	0	0.4	"	6.1901	1.2361	19.97	0.81	24	M	W	σIII	++++
783	4	0.3	"	8.4013	1.6744	19.93	2.90	21	F	B	σIII	+
1160	0	0.3	"	6.9913	1.4316	20.48	1.60	38	F	W	σIII	++++
821	3	0.2	"	4.9843	0.8026	16.10	0.62	22	F	B	σIII	+++
819	5	0.4	"	6.2743	1.3065	20.82	1.70				Latentσ	++++
1171	0	0.4	"	6.6038	1.5035	22.78	0.555				Latentσ	++++
830	10	0.3	"	4.2887	0.7590	17.60	2.66				Latentσ	++++
779	2	0.3	"	6.0570	1.1865	19.59	25.00	20	F	B	σIII	++++
				Interval—10 minutes								
879	7	0.3	10 min.	6.6965	1.3515	20.18	2.22	30	F	B	σIII	++++
1330	0	0.4	"	6.5205	1.4835	22.90	0.339	37	M	W	σIII	++++
545	6	0.3	"	7.1720	1.8439	25.70	0.434	25	F	W	σIII	++++
569	7	0.3	"	7.1950	1.4669	20.37	0.974	28	M	B	σIII	Neg.
885	18	0.4	"	3.1789	0.6379	20.06	0.41	23	F	W	σIII	++++
880	7	0.4	15 min.	5.8771	1.1795	20.06	0.84	30	F	B	σIII	++++
887	11	0.3	"	5.3495	1.1195	20.92	1.12	30	F	W	Latentσ	++++
				Interval—20 minutes								
85	20	0.3	20 min.	6.5990	1.4103	21.37	1.13	26	M	B	σIII	+

17	0	0.3	20 min.	7.2025	1.6202	22.49	1.64	31	M	W	σIII	++++
11	0	0.3	"	9.6731	2.3254	24.11	1.03	26	M	B	σIII	++++
14	0	0.3	"	6.7702	1.3610	20.12	0.734	27	M	W	σIII	++++
89	33	0.3	"	6.6716	1.4807	22.19	0.803	44	M	W	σIII	++++
51	5	0.3	"	7.1329	1.6560	23.19	2.41	40	M	W	σIII	Neg.
67	0	0.3	"	6.5016	1.4698	22.60	2.72	59	M	W	σIII	++++
99	16	0.3	"	7.4866	1.7850	23.84	0.980	39	M	W	σIII	++
52	0	0.3	"	5.1341	1.0925	21.30	1.820	32	M	B	σIII	++++
45	0	0.3	"	6.3080	1.2540	19.87	0.479				Latent	+++
Interval—30 minutes												
570	6	0.3	30 min.	1.7246	0.3874	22.46	1.30	25	F	W	σIII	++++
546	7	0.3	"	6.1466	1.5265	22.62	0.327	28	M	B	σIII	Neg.
886	18	0.3	"	6.8300	1.4626	21.41	1.36	23	F	W	σIII	++++
Interval—40 minutes												
86	20	0.4	40 min.	4.4732	2.9637	21.56	0.310	26	M	B	σIII	+
103	12	0.4	"	6.9396	1.7156	24.72	0.816	26	M	B	σIII	+
18	0	0.4	"	8.5782	1.9800	23.08	1.01	31	M	W	σIII	++++
12	0	0.4	"	7.9380	1.7033	21.46	0.202	26	M	B	σIII	++++
15	0	0.4	"	6.5515	1.2715	19.23	0.295	27	M	W	σIII	++++
90	33	0.4	"	7.6139	1.6366	21.49	1.950	44	M	W	σIII	++++
80	5	0.4	"	4.0572	0.9034	22.26	0.55	40	M	W	σIII	Neg.
68	0	0.4	"	5.3230	1.2279	23.17	1.63	59	M	W	σIII	++++
871	26	0.4	"	4.6550	1.0700	22.98	0.70	40	F	W	σIII	++++
53	0	0.4	"	9.8490	2.5090	25.37	1.95	32	M	B	σIII	++++
46	0	0.3	"	7.3011	1.5970	21.87	1.002				Latent	+++
Interval—50 minutes												
881	7	0.3	50 min.	4.8692	1.0062	20.66	3.21	30	F	B	σIII	++++
884	18	0.3	"	6.2470	1.3413	21.45	1.10	32	F	W	σIII	+++
867	0	0.3	"	4.6837	1.0186	21.74	1.63	36	F	W	σIII	++++
Interval—60 minutes												
47	0	0.3	60 min.	5.1196	1.0386	20.28	1.92				Latent	+++
790		0.4	"	5.4777	1.1260	20.56	0.31	38	M	W	σIII	++++

BLOOD CHART II—Continued

SERIAL NO.	NO. PREV. INJEC.	DOSE OF DRUG	TIME AFTER INJEC.	WT. OF SPECIMEN		PERCENT SOLIDS	AS IN MG. PER 100 GMS. SPEC.	AGE	SEX	COLOR	DIAGNOSIS	WASS.
				MOIST	DRY							
TERTIARY SYPHILIS—Continued												
Interval—60 minutes—Continued												
19	0	0.4	60 min.	5.9900	1.4202	23.70	1.65	31	M	W	σIII	++++
13	0	0.4	"	8.4896	2.1550	25.38	0.14	26	M	B	σIII	++++
16	0	0.4	"	8.3216	1.6096	19.34	1.24	27	M	W	σIII	++++
91	33	0.4	"	7.3397	1.5783	21.00	0.374	44	M	W	σIII	++++
81	5	0.4	"	4.0572	0.9034	22.26	0.123	40	M	W	σIII	Neg.
69	0	0.4	"	7.4177	1.7125	23.08	0.584	59	M	W	σIII	++++
101	26	0.4	"	5.9460	1.4498	24.38	2.76	39	M	W	σIII	++
54	0	0.4	"	7.7222	1.6332	21.15	0.368	32	M	B	σIII	++++
Interval—24 hours												
565	0	0.3	24 hr.	6.8394	1.6110	25.01	0.062				Latentσ	++++
1126	0	0.5	"	6.4708	1.3602	21.02	0.14				Latentσ	++++
591	6	0.4	"	5.0796	1.2257	21.58	0.326	27	M	W	Latent	Neg.
593	0	0.4	"	7.4562	1.7731	23.78	0	?	?	?	Latentσ	++++
595	0	0.4	"	5.4546	1.3046	23.91	0.306	40	M	W	σIII	+++
20	2	0.4	"	8.6254	2.0581	23.86	0.240	22	F	B	σIII	+
Interval—48 hours												
592	1	0.4	"	5.0428	1.1003	21.81	0.708	27	M	W	Latent	Neg.
567	0	0.3	"	8.9410	1.9892	22.24	0.050				Latentσ	++++
1125	0	0.5	"	6.3150	1.3895	22.003	0.108				Latentσ	++++
Interval—3 days												
1102	0	0.5	3 day	4.7600	1.0430	21.91	0.289	30	F	B	Latentσ	++++
Interval—1 week												
105	3	0.3	1 wk.	8.1782	1.5805	19.32	0.632	22	F	B	σIII	++++
106	38	0.4	"	6.6680	1.6260	24.23	1.23	40	M	W	σIII	++

220	9	0.4	1 wk.	6.4374	1.5350	23.84	0.489	32	M	B	σIII	++++
114	9	0.4	"	7.4188	1.5170	20.44	2.30	43	M	W	σIII	++++
1164	1	0.4	"	5.7958	1.2882	22.23	0	32	M	B	σIII	++++
57	23	0.4	"	6.2701	1.3831	22.05	2.17	25	M	W	σIII	++++
2641	2	0.4	"	4.8640	1.0081	20.72	2.47	49	M	B	σIII	++++
56	19	0.4	"	10.0510	2.2360	22.25	0.112	25	M	B	σIII	Neg.
22	5	0.4	"	7.8222	1.6672	21.31	1.19	35	F	B	σIII	++++
72	4	0.4	"	10.2231	2.6010	25.44	0.512	30	M	B	σIII	++++
1281	1	0.4	"	6.6700	1.3800	20.70	0.1089	42	M	B	σIII	++++
1064	0	0.4	"	6.1783	1.4797	23.95	0.48	18	F	W	σIII	+++
107	2	0.3	"	6.9874	1.4511	20.76	0.603	49	F	W	σIII	++++
1234	1	0.4	"	6.3250	1.6057	25.38	0.124		M	W	σIII	++++
104	8	0.3	"	6.9679	1.4014	20.117	0.350		F	W	σIII	++
70	8	0.4	"	2.4438	0.5527	22.617	0.905		M	W	σIII	++++
71	3	0.4	"	6.3126	1.6283	25.63	0.859		M	B	σIII	++++
1059	7	0.4	"	6.7184	1.6059	23.90	1.20		M	W	σIII	++
88	2	0.3	"	6.8856	1.5306	22.24	4.35	24	F	B	σIII	+++
						Interval—9 days						
1174	7	0.3	9 day	5.1884	1.2054	23.23	2.60	40	M	W	σIII	++
						Interval—6 weeks						
982	5	0.3	6 wk.	4.8046	0.9275	19.30	0.32	21	F	B	σIII	+
949	7	0.4	"	6.2034	1.3418	21.64	0.037	30	F	W		++
						Interval—2 months						
928	23	0.4	2 mo.	4.0535	1.0068	24.83	1.60	36	M	W	σIII	++++
924	8	0.4	"	4.8525	1.1449	23.60	Trace	41	M	W	σIII	++++
1073	7	0.4	"	8.3121	1.8055	21.72	0.1108				Latentσ	++++
1104	7	0.4	"	9.4882	2.1802	23.00	Trace				Latentσ	++++
						Interval—6 months						
1048	7	0.4	6 mo.	4.7738	1.1488	24.06	Trace	29	M	B	σIII	++++
						Interval—8 months						
1023	19	0.4	8 mo.		1.6126		0.12	40	M	W	σIII	++++

Blood Chart II—Continued

SERIAL NO.	NO. PREV. INJEC.	DOSE OF DRUG	TIME AFTER INJEC.	WT. OF SPECIMEN MOIST	WT. OF SPECIMEN DRY	PERCENT SOLIDS	AS IN MG. PER 100 GMS. SPEC.	AGE	SEX	COLOR	DIAGNOSIS	WASS.
Tertiary Syphilis—Continued												
Interval—1 year												
926	8	0.4	1 yr.	5.0060	1.1007	21.98	1.69	25	M	W	σIII	Neg.
965		0.4	"	7.1934	1.6285	26.65	0.307	28	F	W	σIII	Neg.
Interval—1½ years												
995	9	0.4	1½ yr.	4.1521	0.9876	23.78	0.202	47	M	W	σIII	Neg.
Congenital Syphilis												
Interval—20 minutes												
58	4	0.4	20 min.	1.7220	7.1608	24.60	1.70	23	M	W	Cong.	++
Interval—40 minutes												
59	4	0.4	40 min.	7.7654	1.9264	24.80	0.311	23	M	W	Cong.	++
Interval—60 minutes												
60	4	0.4	60 min.	6.3416	1.5286	24.10	0.2208	23	M	W	Cong.	++
Interval—24 hours												
596	0	0.3	24 hr.	8.0422	1.6968	21.09	0.029	37	F	W	Cong.	++++
Interval—4 days												
895	11	0.2	4 day	4.1344	0.8055	19.48	1.60	6	F	W	Cong.	++++
Interval—1 week												
832	18	0.2	1 wk.	2.2559	0.4573	20.27	7.20	7	F	W	Cong.	++++
862	17	0.15	"	1.8471	0.3636	19.68	0.27	5	M	W	Cong.	++++
858	18	0.15	"	4.0841	0.8916	21.83	17.0	4	M	W	Cong.	++++
860	19	0.15	"	2.9745	0.6060	20.37	0	2	F	W	Cong.	++++

						Interval—10 months						
947	7	0.4	10 mo.	5.7810	1.6335	28.25	0	23	M	W	Cong.	++
						NON-SYPHILITIC						
						Interval—20 minutes						
61	0	0.4	20 min.	8.0442	1.7604	21.88	1.13				Nonsyph.	Neg.
						Interval—40 minutes						
62	0	0.4	40 min.	8.9446	2.1694	24.25	1.53				Nonsyph.	+
						Interval—60 minutes						
63	0	0.4	60 min.	6.1436	1.4885	24.22	0.336				Nonsyph.	Neg.
						Interval—24 hours						
568	0	0.3	24 hr.	6.1229	1.3580	22.17	1.37				Nonsyph.	Neg.
539	0	0.4	ʻʻ	6.8214	1.5888	23.29	0.0315	37	M	B	Nonsyph.	Neg.
541	0	0.4	ʻʻ	6.5391	1.2941	19.80	0.232	35	F	B	Nonsyph.	Neg.
564	0	0.4	ʻʻ	5.8891	1.2179	20.68	0.205	34	M	W	Nonsyph.	Neg.
1236	0	0.2	ʻʻ	6.3565	1.6753	26.36	Trace	34	M	W	Nonsyph.	Neg.
1329	0	0.3	ʻʻ	5.1400	1.3850	26.92	0.97	26	M	B	Nonsyph.	Neg.
514	0	0.4	ʻʻ	7.5331	1.7206	22.84	0.029	32	M	B	Nonsyph.	Neg.
						Interval—48 hours						
566	0	0.3	48 hr.	6.5830	1.3768	20.89	0.72				Nonsyph.	Neg.
594	0	0.4	ʻʻ	6.5956	1.6691	25.33	0.359				Nonsyph.	Neg.
540	0	0.4	ʻʻ	7.0451	1.7133	24.31	Trace	37	M	B	Nonsyph.	Neg.
550	0	0.4	ʻʻ	5.8422	1.4731	25.59	0.034	29	M	B	Nonsyph.	Neg.
542	0	0.4	ʻʻ	4.3774	0.8864	20.24	0.113	35	F	B	Nonsyph.	Neg.
598	0	0.3	ʻʻ	5.3664	1.1462	21.35	0.072	28	F	B	Nonsyph.	Neg.
1237	0	0.2	ʻʻ	6.8712	1.6636	24.21	0.030	34	M	W	Nonsyph.	Neg.
515	0	0.4	ʻʻ	7.5323	1.8636	24.75	Trace	32	M	B	Nonsyph.	Neg.
						Interval—72 hours						
1238	0	0.2	72 hr.	4.0600	0.9603	23.65	0.052	34	M	W	Nonsyph.	Neg.
						Interval—3 years						
1275	0	0.4	3 yr.	8.1590	1.6604	20.35	0.18	31	M	B	σIII	Neg.

(*Continued from p.* 235.)

INTERVAL—15 MINUTES

LATENT SYPHILIS: 1 case, Wassermann positive.

Amount of arsenic: 1.12 mg. after 0.3 gm. and 11 previous injections, this being the third injection in the second course, at 2 week intervals; female, white, aged 30.

INTERVAL—20 MINUTES

SECONDARY SYPHILIS: 1 case, Wassermann positive.

Amount of arsenic: 0.271 mg. after 0.4 gm. and 7 previous injections, all of which had been given within a month before, female, black, aged 19.

TERTIARY SYPHILIS: 9 cases, 8 with positive Wassermann, 1 negative Wassermann.

No. of previous injections: 0-33.

Dose: 0.4 gm.

Smallest amount of arsenic: 0.734 mg. after 0.4 gm. and 0 previous injections; male, white, aged 27.

Largest amount of arsenic: 2.72 mg. after 0.4 gm., no previous injections, male, white, aged 59.

Average amount of arsenic: 1.47 mg.

LATENT SYPHILIS: 1 case, Wassermann positive.

Amount of arsenic: 0.479 mg. after 0.3 gm., no previous injections; female, white, adult.

CONGENITAL SYPHILIS: 1 case; Wassermann positive.

Amount of arsenic: 1.7 mg., after 0.4 gm. and 4 previous weekly injections, male, white, aged 23.

NONSYPHILITIC: 1 case; Wassermann negative.

Amount of arsenic: 1.13 mg., after 0.4 gm., no previous injections, male, white, adult.

INTERVAL—30 MINUTES

TERTIARY SYPHILIS: 3 cases; 2 with positive Wassermann; 1 negative.

No. of previous injections; 6-18.

Dose: 0.3 gm.

Smallest amount of arsenic: 0.327 mg. after 0.3 gm. and 7 previous injections eight months before; male, black, aged 28.

Largest amount of arsenic: 1.36 mg. after 0.3 gm. and 18 previous injections, this being the 6th at 2 week intervals after a rest of nearly 3 years; female, white, aged 23.

Average amount of arsenic: 0.995 mg.

INTERVAL—40 MINUTES

TERTIARY SYPHILIS: 10 cases; 9 with positive Wassermann; 1 negative.

No. of previous injections: 0-33.

Dose: 0.4 gm.

Smallest amount of arsenic: 0.202 mg. after 0.4 gm. no previous injections; male, black, aged 26.

Largest amount of arsenic: 1.95 mg. after 0.4 gm. and 0 previous injections; male, black, aged 32.

Average amount of arsenic: 0.87 mg.

LATENT SYPHILIS: 1 case; Wassermann positive.

Amount of arsenic: 1.002 mg. after 1.3 gm., no previous injections; adult male, white.

CONGENITAL SYPHILIS: 1 case; Wassermann positive.

Amount of arsenic: 0.311 mg. after 0.4 gm. and 4 previous weekly injections; male, white, aged 23.

NONSYPHILITIC: 1 case; Wassermann negative.

Amount of arsenic: 1.53 mg. after 0.4 gm. and no previous injections; male, white adult.

INTERVAL—50 MINUTES

TERTIARY SYPHILIS: 3 cases; Wassermann positive.

No. of previous injections: 0-18.

Dose: 0.3 gm.

Smallest amount of arsenic: 1.1 mg. after 0.4 gm. and 18 previous injections, the present being the 7th in a new course at weekly intervals; female, white, aged 32.

Largest amount of arsenic: 3.21 mg. after 0.4 gm. and 7 previous injections, the last 6 mos. before; female, black, aged 30.

Average amount of arsenic: 1.98 mg.

INTERVAL—60 MINUTES

TERTIARY SYPHILIS: 9 cases; 8 with positive Wassermann; 1 negative.

No. of previous injections: 0-33.

Dose: 0.4 gm.

Smallest amount of arsenic: 0.062 mg. after 0.3 gm.; no previous injections at 3 and 4 weekly intervals; male, white, aged 40.

Largest amount of arsenic: 2.76 mg. after 0.4 gm. and 26 previous injections: male, white, aged 39.

Average amount of arsenic in this group: 0.84 mg.

LATENT SYPHILIS: 1 case; Wassermann positive.

Amount of arsenic: 1.920 mg. after 0.3 gm. and no previous injections; male, white, adult.

CONGENITAL SYPHILIS: 1 case; Wassermann positive.

Amount of arsenic 0.2208 mg. after 0.4 gm. and 4 weekly injections; male, white, aged 23.

NONSYPHILITIC: 1 case; Wassermann negative.

Amount of arsenic: 0.336 mg. after 0.4 gm. and 0 previous injections; adult, male, white.

INTERVAL—24 HOURS

SECONDARY SYPHILIS: 2 cases; Wassermann positive.

Smaller amount of arsenic: 0 after 0.4 gm., no previous injections; male, black, aged 19.

Larger amount of arsenic 0.0477 mg. after 0.4 gm. and no previous injections; male, black, aged 24.

Average amount of arsenic: 0.0240 mg.

TERTIARY SYPHILIS: 2 cases; Wassermann positive.

Smaller amount of arsenic: 0.24 mg. after 0.4 gm. and 2 previous injections, female, black, aged 22.

Larger amount of arsenic: 0.306 mg. after 0.4 gm. and 2 previous injections; male, white, aged 40.

Average amount of arsenic in this group: 0.27 mg.

LATENT SYPHILIS: 4 cases, 3 with positive Wassermann, 1 negative.

No. of previous injections: 0 in 2 cases; 1 had 6 neosalvarsans 6 years before.

Dose: 2 cases 0.3 gm., 1 case 0.5 gm.

Smallest amount of arsenic: 0.062 mg. after 0.3 gm.; no previous injections; female, black, aged 28.

Largest amount of arsenic: 0.326 mg. after 0.4 gm., had received 6 injections of neosalvarsan 6 years before; male, white, aged 27.

Average arsenic value: 0.13 mg.

NONSYPHILITIC: 7 cases; Wassermann negative.

No. of previous injections: 0.

Dose: 3 cases, 0.3 gm.; 15 cases, 0.4 gm.

Smallest amount of arsenic: Trace after 0.2 gm., no previous injections; male, white, aged 34.

Largest amount of arsenic: 1.37 mg. after 0.3 gm., no previous injections, male, black, aged 26.

Average amount of arsenic: 0.405 mg.

INTERVAL—48 HOURS

SECONDARY SYPHILIS: 2 cases; Wassermann positive.

Smaller amount of arsenic: 0.253 mg. after 0.3 gm. and no previous injections; female, white, aged 20.

Larger amount of arsenic: (same patient) 1.03 mg. after 0.3 gm. and 1 previous injection 2 days before, female, white, aged 20.

Average amount of arsenic in this group: 0.64 mg.

LATENT SYPHILIS: 3 cases, 2 Wassermann positive, 1 Wassermann negative.

Smaller amount of arsenic: 0.050 mg. after 0.3 gm. and no previous injection; male, white, adult.

Larger amount of arsenic: 0.708 mg. after 0.4 gm. and 1 previous injection; male, white, aged 27.

Average amount of arsenic: 0.271 mg.

NONSYPHILITIC: 8 cases; Wassermann negative.

No. of previous injections: 0.

Dose: 1 case, 0.2 gm., 2 cases, 0.3 gm.; 5 cases, 0.4 gm.

Smallest amount of arsenic: Trace in 2 cases; 1 after 0.4 gm., male, black, aged 37; the other after 0.4 gm.; male, black, aged 32.

Largest amount of arsenic: 0.72 mg. after 0.4 gm. and no previous injections; male, yellow, aged 30.

Average amount of arsenic: 0.166 mg.

INTERVAL—72 HOURS

TERTIARY SYPHILIS: 1 case; Wassermann positive.

Amount of arsenic: 0.289 mg. after 0.5 gm., no previous injections; female, black, aged 30.

NONSYPHILITIC: 1 case: Wassermann negative.

Amount of arsenic: 0.052 mg. after 0.2 gm., no previous injections; male, white, aged 34.

INTERVAL—4 DAYS

SECONDARY SYPHILIS: 1 case; Wassermann positive.

Amount of arsenic: trace after 0.4 gm. and no previous injections; male, black, aged 26.

INTERVAL—5 DAYS

SECONDARY SYPHILIS: 1 case; Wassermann positive.

Amount of arsenic: 0.548 mg. after 0.3 gm. and 4 injections at weekly intervals; female, white, aged 21.

INTERVAL—1 WEEK

PRIMARY SYPHILIS: 1 case; Wassermann negative.

Amount of arsenic: 3.89 mg. after 0.4 gm. and 14 previous injections, the last the 6th of the second course at weekly intervals; male, white, aged 40.

SECONDARY SYPHILIS: 3 cases; 2 with positive Wassermann; 1 negative.

Smallest amount of arsenic: 0.023 mg. after 0.3 gm. and 1 injection the week previous; female, white, aged 22.

Largest amount of arsenic: 3.88 mg. after 0.4 gm. and 30 previous injections; female, white, aged 28.

Average amount of arsenic for this group: 2.01 mg.

TERTIARY SYPHILIS: 18 cases, 12 with positive Wassermann; 1 negative.

No. of previous injections: 1–38.

Dose: 3 cases, 0.3 gm.; 15 cases, 0.4 gm.

Smallest amount of arsenic: 1 after 0.4 gm. and 1 previous injection the week before; male, black, aged 32.

Largest amount of arsenic: 2.47 mg. after 0.4 gm. and 2 previous injections at weekly intervals; male, black, aged 49.

Average amount of arsenic in this group: 0.86 mg.

INTERVAL—9 DAYS

TERTIARY SYPHILIS: 1 case; Wassermann positive.

Amount of arsenic 0.260 mg. after 0.4 gm. and 7 previous injections; male, white, aged 40.

INTERVAL—6 WEEKS

TERTIARY SYPHILIS: 2 cases, Wassermann positive.

Smaller amount of arsenic: 0.037 after 0.4 gm. and 7 previous injections, taken weekly, female, white, aged 30.

Larger amount of arsenic: 0.32 mg. after 0.3 gm. and 5 previous injections, taken irregularly; female, black, aged 21.

Average amount of arsenic: 0.178 mg.

INTERVAL—2 MONTHS

SECONDARY SYPHILIS: 4 cases; Wassermann positive.

Smallest amount of arsenic: 0.12 mg. after 0.4 gm. and 23 previous injections, this one being last of third course, weekly intervals; male, white, aged 34.

Largest amount of arsenic: 0.810 mg. after 0.4 gm. and 13 previous injections, the second course being irregularly taken every 2 or 3 months; male, white, aged 41.

Average amount of arsenic: 0.382 mg.

TERTIARY SYPHILIS: 2 cases; Wassermann positive.

Smaller amount of arsenic: trace after 0.4 gm. and 8 previous injections; male, white, aged 41.

Larger amount of arsenic: 1.6 mg. after 0.4 gm. and 23 previous injections; male, white, aged 36.

Average amount of arsenic: 0.8 mg.

LATENT SYPHILIS: 2 cases; Wassermann positive.

Smaller amount of arsenic: trace after 0.4 gm. and 7 previous weekly injections, male, white, adult.

Larger amount of arsenic: 0.1108 mg. after 0.4 gm. and 7 previous injections, at intervals of months; male, white, adult.

Average amount of arsenic: 0.0554 mg.

INTERVAL—6 MONTHS

TERTIARY SYPHILIS: 1 case; Wassermann positive.

Amount of arsenic: trace after 0.4 gm. and 7 previous injections; male, black, aged 29.

INTERVAL—8 MONTHS

TERTIARY SYPHILIS: 1 case; Wassermann positive.

Amount of arsenic: 0.12 mg. after 0.4 gm. and 19 previous injections, the last 8 at weekly intervals; male, white, aged 40.

INTERVAL—10 MONTHS

CONGENITAL SYPHILIS: 1 case; Wassermann positive.

No arsenic present after 0.4 gm. and 7 previous injections, at weekly intervals; male, white, aged 23.

INTERVAL—1 YEAR

TERTIARY SYPHILIS: 2 cases; Wassermann negative.

Smaller amount of arsenic: 0.307 mg. after 0.4 gm. irregular treatment 1 year previously; female, white, aged 28.

Larger amount of arsenic: 1.69 mg. after 0.4 gm. and 8 previous injections; male, white, aged 25.

Average amount of arsenic: 0.99 mg.

INTERVAL—1½ YEARS

TERTIARY SYPHILIS: 1 case; Wassermann negative.

Amount of arsenic: 0.202 mg. after 0.4 gm. and 9 previous injections; male, white, aged 47.

INTERVAL—2 YEARS

SECONDARY SYPHILIS: 1 case; Wassermann negative.

Amount of arsenic: 0.15 mg. after 0.4 gm. Had had 2 courses of salvarsan 2 years ago; male, white, aged 32.

INTERVAL—3 YEARS

TERTIARY SYPHILIS: 1 case; Wassermann negative.

Amount of arsenic; 0.18 mg. after 0.4 gm. Patient had had only one injection 3 years before; male, black, aged 31.

Table III

All specimens of blood included in this generalized table were obtained at the various intervals with an accuracy of 30 seconds. This table is used as a control upon the values found in Table I and the specimens were taken at an interval of more than six months after the previous tables. Total number of specimens 258.

Blood Chart III

SERIAL NO.	NO. PREV. INJEC.	DOSE OF DRUG	TIME AFTER INJEC.	WT. OF SPECIMEN MOIST	WT. OF SPECIMEN DRY	PERCENT SOLIDS	AS IN MG. PER 100 GMS. SPEC.	AGE	SEX	COLOR	DIAGNOSIS	WASS.
2150	4	0.4	Immed.	5.1393	1.0936	21.27	1.37	28	M	W	σII	++++
2655	1	0.4	"	3.3187	0.7357	22.10	5.66	39	M	W	σIII	Neg.
2623	8	0.4	"	3.8174	0.6838	17.91	21.9	38	M	W	σII	++++
2669	52	0.4	"	4.5900	0.9517	20.73	2.10	40	M	W	σIII	++++
2694	13	0.4	"	4.7921	0.9969	20.80	1.003	45	M	W	σIII	+++
2687	45	0.4	"	4.1605	0.9155	22.04	2.18	33	M	W	σIII	Neg.
2625	3	0.4	"	4.9020	0.9003	18.37	2.96	41	M	W	σIII	+++
2661	15	0.4	"	3.2521	0.6236	19.17	0.801	34	M	W	σIII	++++
2168	17	0.4	"	4.0161	0.9102	22.66	0.366	18	M	B	σII	++++
2158	28	0.4	"	5.6377	1.3453	23.86	1.85	30	M	W	σIII	+++
2657	32	0.4	"	5.5928	1.1417	20.41	7.007	30	M	W	σIII	+++
2172	6	0.4	"	6.0391	1.4688	24.32	1.02	23	M	B	σII	++
2174	4	0.4	"	5.0100	1.0866	21.68	1.83	30	M	W	σII	++++
2692	45	0.4	"	5.1711	1.2514	22.07	1.99	45	M	W	σIII	++++
2627	13	0.4	"	4.7223	1.0665	22.58	1.40	20	M	W	Cong.	++++
2148	1	0.4	"	2.3397	0.5263	22.409	6.33	30	M	W	σI	Neg.
2170	3	0.4	"	5.6101	1.2215	21.77	3.68	23	M	W	σIII	+++
2176	8	0.4	"	3.0898	0.6406	20.73	0.891	?	M	W	σII	++++
2689	2	0.4	"	4.6314	1.0409	22.47	5.76	?	M	W	Latent	+++
2640	14	0.4	"	6.6982	1.4665	21.89	4.09	23	M	W	σIII	++++
2636	2	0.4	"	3.6687	0.7935	21.08	5.04	20	M	B	σII	++++
2659	1	0.4	"	2.7391	0.5705	20.82	5.84	30	M	W	σII	++++
2164	1	0.3	"	2.6259	0.5308	20.21	0.289	37	M	W	σIII	++++
2160	31	0.4	"	3.3800	0.7050	20.85	3.54	38	M	B	σIII	++++
2162	2	0.4	"	5.9649	1.3579	22.79	1.76	36	M	W	σIII	++++
2667	9	0.4	"	4.3226	0.8929	20.65	2.79	26	M	W	σIII	++++
2696	14	0.4	"	5.0196	1.1713	23.33	1.49	53	M	W	σIII	++++

2653	19	0.4	“	4.0093	0.8438	21.04	5.92	25	M	W	σII	++++
2156	1	0.4	“	3.4133	0.7020	20.56	5.69	35	M	B	σIII	++++
2684	50	0.4	“	4.1825	0.8934	21.36	2.23	27	M	W	σIII	+++
2665	68	0.4	“	4.6634	1.0506	22.52	5.71	42	M	W	σIII	Neg.
2651	29	0.4	“	3.1359	0.6544	20.54	6.11	42	M	B	σIII	+
2671	10	0:4	“	4.2736	0.9177	21.47	5.44	24	M	W	σII	++++
2166	2	0.4	“	2.8745	0.6400	22.26	0.3905	29	M	W	σII	++++
2631	0	0.3	“	4.5829	1.0167	22.18	4.91	43	M	W	σIII	++++
2700	14	0.4	“	4.1364	0.8635	20.87	11.5	25	M	W	σIII	++++
2618	6	0.4	“	5.0372	0.9940	19.73	4.02	54	M	W	σIII	++++
2617	19	0.4	“	5.4092	1.2159	22.47	2.46	40	M	W	σII	++++
2686	2	0.4	“	5.4680	1.2034	22.19	16.6	34	M	W	σIII	+
2628	18	0.3	“	5.5794	1.2950	23.21	1.54	29	M	W	σIII	+
2154	8	0.4	“	4.1106	0.9528	23.17	2.62	23	M	W	σII	++++
2638	1	0.4	“	5.3865	1.1601	21.53	4.30	34	M	W	σIII	++++
2682	10	0.4	“	5.9795	1.2850	21.48	7.77	30	M	B	σII	++++
2152	8	0.4	“	5.1863	1.0351	19.95	2.41	27	M	W	σII	+
2698	4	0.4	“	4.7282	1.0538	22.28	0.948	49	M	W	σIII	++++
2614	8	0.4	“	5.7946	1.3271	22.90	7.53	33	M	W	σIII	++++
2642	3	0.4	“	5.0682	0.9430	18.60	5.30	49	M	B	σIII	++++
2633	6	0.4	“	4.2410	0.9660	22.77	3.45	25	M	W	σII	+++
2621	10	0.4	“	5.4476	1.1494	21.09	4.35	31	M	W	σIII	Neg.
2663	6	0.4	“	4.5641	0.8870	19.43	6.70	23	M	W	σIII	++++
2644	1	0.4	“	4.7885	1.0496	21.91	1.90	22	M	B	σIII	Neg.
2395	2	0.4	5 min.	3.8865	0.8789	22.62	0.113	22	M	W	σI	Neg.
2393	14	0.4	“	5.2987	1.1306	21.33	0.265	45	M	W	σIII	++++
2400	38	0.4	“	3.8630	0.8140	21.08	0.351	28	M	B	σII	Neg.
2399	4	0.4	“	4.3645	0.9695	22.21	1.54	32	M	W	σIII	++++
2392	3	0.4	“	1.9284	0.4579	23.74	1.45	23	M	B	σII	++
2387	13	0.4	“	4.3340	0.9405	21.70	0.850	23	M	W	σIII	++++
2390	25	0.4	“	4.4463	1.0250	23.05	0.195	20	M	W	σII	++++
2398	3	0.3	“	1.0162	0.2198	21.63	1.51	45	M	W	σIII	++
2391	20	0.4	“	4.6547	1.0734	23.08	1.49	35	M	B	σIII	++
2397	13	0.3	“	4.9715	0.9801	19.72	5.101	26	F	W	σIII	++
2389	13	0.4	“	3.9594	0.8943	22.58	0	40	M	W	σII	++++
2386	14	0.3	“	3.0540	0.6624	21.68	5.28	20	F	W	σIII	+++
2396	8	0.4	“	4.8146	1.0360	21.54	1.28	31	M	W	σI	Neg.
2394	6	0.4	“	4.2590	0.8970	21.06	0.222	27	M	W	σII	++++

BLOOD CHART III—Continued

SERIAL NO.	NO. PREV. INJEC.	DOSE OF DRUG	TIME AFTER INJEC.	WT. OF SPECIMEN		PERCENT SOLIDS	AS IN MG. PER 100 GMS. SPEC.	AGE	SEX	COLOR	DIAGNOSIS	WASS.
				MOIST	DRY							
2484	15	0.4	10 min.	3.9878	0.8884	22.27	3.001	22	M	W	σII	++++
2406	5	0.4	"	3.6288	0.7460	20.56	.066	17	M	W	Cong.	+++
2408	4	0.4	"	2.8255	0.6218	22.01	0	56	M	B	σIII	++++
2401	6	0.3	"	3.5505	0.6373	18.00	0	25	F	B	Cong.	++++
2404	20	0.4	"	3.7929	0.8496	22.39	0	35	M	W	σII	Neg.
2492	7	0.4	"	4.3140	0.9617	22.29	0	30	M	B	σIII	++++
2503	21	0.4	"	4.1097	0.9112	22.17	2.19	27	M	W	σII	++++
2405	3	0.3	"	......	0.5759	.....	0.173	?	F	W	σIII	++++
2410	2	0.3	"	4.2334	0.9027	21.32	0.0553	22	F	W	Cong.	+++
2403	18	0.3	"	3.9094	0.8165	20.63	3.67	40	F	W	σII	Neg.
2485	14	0.4	"	4.5045	1.0275	22.81	0.583	24	M	W	σIII	+
2407	11	0.4	"	2.7768	0.5981	21.53	0.167	38	M	W	σIII	++++
2509	3	0.4	"	3.4122	0.7889	23.12	3.80	23	M	W	σII	++++
2402	1	0.3	"	4.0135	0.8335	20.76	0.599	21	F	W	σIII	++++
2506	15	0.4	"	4.5319	0.9975	22.01	1.50	40	M	W	σII	++++
2409	11	0.3	"	3.9604	0.7824	19.76	0.255	?	F	B	Latent	Neg.
2501	3	0.4	"	5.0434	1.1076	21.96	0.902	49	M	W	σIII	++++
2488	9	0.4	15 min.	4.6543	0.9114	19.58	0.219	41	M	W	σIII	++++
2502	3	0.4	"	3.0015	0.6630	22.08	3.77	43	M	B	σIII	++++
2429	6	0.4	"	4.7856	0.9728	20.32	0.102	56	M	B	σIII	++++
2411	4	0.4	"	4.7540	1.0583	22.26	0.094	32	M	B	σIII	+
2412	3	0.4	"	5.9600	1.4259	23.92	0.526	34	M	W	σIII	++++
2435	11	0.3	"	5.2400	1.1278	21.52	0.086	27	F	W	σIII	++++
2547	5	0.4	"	4.8095	1.0192	21.19	0.588	24	M	W	σIII	++++
2430	0	0.4	"	4.7166	0.9241	19.59	0.270	20	M	B	σI	Neg.
2504	14	0.4	"	4.1295	0.8438	20.43	3.15	32	M	B	σIII	++
2433	8	0.4	"	4.7238	0.9746	20.63	0	22	M	W	σIII	++++
2431	11	0.4	"	4.8299	0.9922	20.54	1.61	27	M	W	σII	++++
2543	1	0.4	"	5.5583	1.2088	21.74	0.827	50	M	B	σIII	++++
2413	2	0.4	"	3.9212	0.8956	22.84	3.72	49	M	W	σIII	Neg.

2438	2	0.2	20 min.	5.5429	1.0704	19.31	0.467	36	F	B	σIII	+++
2548	7	0.2	“	3.8702	0.8059	20.79	0	46	F	B	σIII	++++
2442	0	0.3	“	4.2692	0.9592	22.46	0.208	27	F	W	σIII	++++
2428	11	0.3	“	4.8415	1.0305	21.28	1.94	35	F	W	σIII	++++
2541	2	0.3	“	4.9275	0.8660	17.57	1.15	35	F	W	σII	++++
2440	1	0.3	“	4.6932	0.9476	20.19	0.105	30	F	B	σIII	++
2446	10	0.3	“	4.5666	0.9541	20.89	1.57	51	F	W	σIII	++++
2439	16	0.3	“	6.8300	1.3139	19.23	0.076	19	F	B	Cong.	++++
2437	0	0.3	“	5.0569	1.0708	21.17	0.186	39	F	W	σIII	++++
2447	2	0.3	“	5.0052	1.0156	20.29	0.098	29	F	W	σIII	++++
2445	0	0.2	“	4.4766	0.9062	20.24	0.220	19	F	B	σIII	++++
2441	3	0.2	“	5.6554	1.1267	19.92	0.266	30	F	B	σIII	+++
2542	7	0.3	“	4.8327	1.0227	21.16	1.46	33	M	W	σIII	++++
2545	1	0.3	“	4.8861	1.0130	20.73	0.658	39	F	W	σIII	++++
2544	1	0.4	“	4.8356	0.8552	17.66	3.50	23	M	B	σIII	++++
2489	6	0.4	30 min.	4.0650	0.8968	22.06	0.055	38	M	W	σII	++++
2505	40	0.4	“	3.8975	0.8750	22.45	0.342	28	M	B	σII	Neg.
2495	0	0.4	“	4.8234	0.9771	20.25	1.53	37	M	B	σII	++++
2510	4	0.4	“	3.1297	0.7201	23.00	0.694	23	M	B	σII	++
2487	56	0.4	“	4.6136	1.0427	22.60	0.767	28	M	W	σIII	++++
2444	3	0.4	“	4.2202	0.9102	21.56	0	?	M	B	σIII	++++
2546	9	0.3	“	5.0021	0.9620	19.23	2.59	27	F	W	σIII	++++
2443	0	0.3	“	4.1226	0.8142	19.74	0.122	?	M	W	Latentσ	++++
2491	4	0.4	“	4.1200	0.8685	20.59	0.345	30	M	B	σII	++++
2508	14	0.4	“	3.6134	0.8034	22.23	1.55	37	M	B	σIII	++++
2486	0	0.4	“	4.4919	0.9930	22.106	0.1007	25	M	W	σII	+++
2434	53	0.4	“	3.3079	0.7694	23.26	0	40	M	W	σIII	Neg.
2311	0	0.3	1 hr.	7.0768	1.5022	21.22	0	55	F	W	σIII	++++
2603	2	0.3	“	5.9335	1.1471	19.34	Trace	30	F	W	σIII	++++
2602	13	0.4	“	4.6688	0.9903	21.21	0.252	43	M	W	σIII	++++
2597	22	0.3	“	7.1950	1.4590	20.27	0.685	40	F	W	σIII	+++
2594	0	0.3	“	5.4069	1.0999	20.34	1.81	33	F	B	σIII	++++
2312	3	0.3	“	5.3730	1.0265	19.10	Trace	25	F	B	σIII	++++
2593	16	0.3	“	4.5558	1.0068	22.09	0.331	34	F	W	σIII	++++
2599	2	0.4	“	7.3056	1.5361	21.02	0.13	?	M	W	Latentσ	++++

BLOOD CHART III—Continued

SERIAL NO.	NO. PREV. INJEC.	DOSE OF DRUG	TIME AFTER INJEC.	WT. OF SPECIMEN MOIST	DRY	PERCENT SOLIDS	AS IN MG. PER 100 GMS. SPEC.	AGE	SEX	COLOR	DIAGNOSIS	WASS.
2598	13	0.3	1 hr.	4.6845	1.0000	21.34	0.200	38	F	W	σIII	++++
2596	10	0.3	“	5.6179	1.1881	21.14	0.841	51	F	W	σIII	++++
2600	13	0.4	“	6.4102	1.4557	22.70	0.687	?	M	W	Latent	Neg.
2595	4	0.4	“	8.1402	1.7480	21.47	1.14	?	M	B	Latent	++++
2490	14	0.4	“	3.9496	0.9384	23.75	0.106	37	M	B	σIII	++++
2309	1	0.3	“	4.9211	0.9198	18.69	0.434	24	F	B	σIII	++++
2601	0	0.4	“	5.6296	1.2643	22.45	0.988	22	M	B	σIII	Neg.
2521	9	0.4	“	......	0.7295	.....	1.02	36	M	W	Latent	++++
2329	2	0.3	2 hr.	4.3720	0.6603	15.10	0.454	?	F	W	σIII	++++
2310	21	0.4	“	4.3928	0.9073	20.63	0.52	42	M	W	σIII	+
2248	10	0.3	24 hr.	3.9950	0.9178	22.97	0	28	F	B	σIII	Neg.
2189	2	0.3	“	3.7317	0.7187	19.25	0.139	22	F	W	Cong.	++++
2190	0	0.4	“	3.0162	0.6826	22.63	0.293	17	M	W	Cong.	++++
2241	0	0.4	“	4.2419	0.9457	22.29	1.32	43	M	B	σIII	++++
2374	12	0.4	“	4.9899	1.1969	23.98	0.167	32	M	W	σIII	Neg.
2350	9	0.4	“	4.3968	0.9582	21.79	0.313	30	M	W	σI	Neg.
2239	0	0.4	“	4.0568	0.9067	22.35	0.367	?	M	W	Nonsyph.	Neg.
2278	9	0.4	“	3.1472	0.7237	22.99	0	29	M	W	Nonsyph.	Neg.
2187	31	0.4	“	4.1090	0.9537	23.21	0.052	28	M	B	σIII	++++
2188	0	0.4	“	3.5624	0.7829	21.97	1.27	36	M	W	σII	++++
2376	0	0.3	“	3.5988	0.8196	22.77	0.488	30	M	B	σIII	Neg.
2414	1	0.4	“	4.5919	1.0784	23.48	0	40	M	B	σIII	Neg.
2416	0	0.4	“	4.8467	0.9762	20.14	0.409	15	M	W	Nonsyph.	Neg.
2192	6	0.3	“	3.6535	0.7320	20.03	0.273	14	F	W	σI	Neg.
2452	1	0.4	“	4.2695	1.0269	24.05	0.194	20	M	W	Latent	++++
2191	5	0.4	“	3.7930	0.8430	21.98	0.0593	?	M	W	Latent	++++
2247	1	0.3	“	3.9596	0.8444	21.32	0.355	24	F	B	σIII	++++
2286	8	0.3	48 hr.	5.8200	1.2083	20.42	0.0413	?	M	W	Latent	+
2242	0	0.4	“	3.9105	0.8638	22.08	0.463	43	M	B	σIII	++++
2330	12	0.4	“	5.3253	1.2069	22.66	0.331	26	M	W	σIII	++++

2375	12	0.4	48 hr.	4.3885	0.9858	22.46	0.101	32	M	W	σIII	Neg.
2245	8	0.25	“	3.8874	0.9175	23.601	0.435	15	M	W	Cong.	++++
2240	0	0.4	“	3.9144	0.7659	19.56	0.0652	?	M	W	Nonsyph.	Neg.
2279	0	0.4	“	4.0509	0.8950	22.09	0	29	M	W	Nonsyph.	Neg.
2246	3	0.4	“	4.7892	1.0539	22.005	Trace	21	M	B	σIII	++++
2238	7	0.4	“	3.1510	0.6269	19.89	0.0797	35	M	B	σIII	++++
2333	4	0.4	“	3.9328	0.9185	23.35	2.72	36	M	W	σII	++++
2288	0	0.4	“	6.9265	1.6049	23.17	0.187	54	M	W	σIII	++++
2282	?	0.4	“	1.7931	0.3881	21.64	1.03	?	F	W	Latent	++++
2415	1	0.4	“	4.6346	1.1490	24.78	1.39	40	M	B	σIII	Neg.
2417	0	0.4	“	4.7091	1.0506	22.31	0.438	15	M	W	Nonsyph.	Neg.
2453	1	0.4	“	4.4223	0.9930	22.45	1.006	20	M	W	Latent	++++
2289	2	0.4	“	6.9819	1.5779	22.59	0.383	44	M	B	σIII	++++
2327	10-15	0.4	“	4.9505	1.0713	21.64	0.932	37	M	W	σIII	Neg.
2287	8	0.3	72 hr.	3.8418	0.8250	20.47	0.484	?	M	W	Latent	+
2243	0	0.4	“	4.9344	1.0934	22.15	1.21	43	M	B	σIII	++++
2572	1	0.4	“	2.9263	0.6758	22.81	0	37	M	B	σII	++++
2570	6	0.3	“	4.9321	1.0140	20.56	0	22	M	W	σIII	++++
2280	0	0.4	“	5.4121	1.2051	22.26	0.995	29	M	W	Nonsyph.	Neg.
2574	20	0.3	“	4.9267	0.9356	18.99	0.320	28	F	B	Latent	++++
2575	0	0.4	“	5.3932	1.2221	22.66	0	38	M	B	σI	Neg.
2315	4	0.4	“	4.9940	1.1076	22.17	1.80	54	M	W	Latent	++++
2573	11	0.3	“	5.1727	1.1131	21.51	0.179	35	F	W	σIII	++++
2377	0	0.3	“	4.3300	0.9328	21.54	0.857	30	M	B	σIII	Neg.
2283	?	0.4	“	3.6424	0.7748	21.27	0	?	F	W	Latent	++++
2507	1	0.4	“	4.8296	0.9089	18.81	0.366	20	M	W	σII	++++
2328	10-15	0.4	“	3.8255	0.8780	22.95	1.13	37	M	W	σIII	Neg.
2313	3	0.4	“	4.2737	0.9109	21.31	0.109	31	M	W	σI	Neg.
2571	40	0.3	“	6.3780	1.3738	21.54	0.036	38	F	W	σIII	++++
2149	4	0.4	“	4.1871	0.8336	19.908	0.239	28	M	W	σII	++++
2147	1	0.4	“	3.9069	0.9544	24.43	0.209	30	M	W	σI	Neg.
2523	0	0.4	96 hr.	5.2517	1.0405	19.81	0.0961	25	F	W	Nonsyph.	Neg.
2324	9	0.4	“	3.8716	0.7956	20.54	1.67	28	M	W	σII	++++
2522	7	0.3	“	5.3332	1.0639	19.94	0.234	17	M	W	Cong.	++++
2325	3	0.4	“	2.9770	0.6440	21.62	0.310	32	M	W	σIII	++++

BLOOD CHART III—Continued

SERIAL NO.	NO. PREV. INJEC.	DOSE OF DRUG	TIME AFTER INJEC.	WT. OF SPECIMEN		PERCENT SOLIDS	AS IN MG. PER 100 GMS. SPEC.	AGE	SEX	COLOR	DIAGNOSIS	WASS.
				MOIST	DRY							
2195	0	0.4	96 hr.	3.6123	0.7900	21.86	0.126	32	M	W	σIII	++++
2244	0	0.4	“	5.1086	1.1168	21.07	0	34	M	W	Nonsyph.	Neg.
2525	5	0.4	“	3.9005	0.8154	20.90	1.83	34	M	W	σIII	++++
2237	2	0.4	“	5.5441	1.1725	22.24	0	36	M	W	σIII	++++
2524	21	0.4	“	5.7924	1.1655	20.12	0.343	42	M	W	σIII	+
2197	40	0.3	“	3.9443	0.8368	21.21	0	49	F	W	σIII	++++
2332	20	0.4	“	5.2686	1.1465	21.76	0.0871	49	M	W	σIII	++++
2194	2	0.4	“	4.8391	1.1811	24.61	0.169	34	M	W	σIII	++++
2193	9	0.4	“	4.1680	0.9358	22.45	0	22	M	W	σIII	++++
2196	0	0.3	“	4.1503	0.8708	20.98	1.14	?	F	W	Latent	++++
2326	0	0.4	“	4.0480	0.8529	22.06	0.117	31	M	W	Nonsyph.	Neg.
2331	1	0.4	“	3.6858	0.7678	20.83	1.30	27	M	W	σII	++++
2654	0	0.4	5 day	2.9021	0.6631	22.84	2.41	39	M	W	σIII	Neg.
2660	14	0.4	“	3.7574	0.7553	20.10	0.264	34	M	W	σIII	++++
2666	8	0.4	“	4.3480	0.9123	20.98	0	26	M	W	σIII	++++
2643	0	0.4	“	3.7444	0.8000	21.36	0.750	22	M	B	σIII	Neg.
2649	7	0.3	1 wk.	4.5471	0.9818	21.59	0.305	15	M	W	Cong.	++++
2626	12	0.4	“	5.5464	1.2645	22.79	0.988	20	M	W	Cong.	++++
2169	2	0.4	“	3.4027	0.7489	22.008	0.133	23	M	W	σIII	+++
2175	8	0.4	“	2.1695	0.4711	21.71	0.424	?	M	W	σII	++++
2635	2	0.4	“	4.4885	0.9616	21.42	1.03	20	M	B	σII	++++
2658	0	0.4	“	4.8198	0.9952	20.64	1.205	30	M	W	σII	++++
2163	0	0.4	“	4.9726	1.1623	23.37	1.14	37	M	W	σIII	+++
2634	3	0.3	“	5.7875	1.2948	22.37	0.386	47	M	W	σIII	++++
2683	49	0.4	“	5.6911	1.2382	21.75	0.161	27	M	W	σIII	+++
2650	28	0.4	“	3.8474	0.8971	23.31	1.11	42	M	B	σIII	+
2670	9	0.4	“	5.0662	1.2127	23.93	0.206	24	M	W	σII	++++
2165	1	0.4	“	3.9883	0.9672	24.25	0	29	M	W	σII	++++
2619	5	0.4	“	6.4963	1.2887	19.83	0.931	54	M	W	Latent	++++

2685	1	0.4	1 wk.	5.0507	1.1249	22.27	4.14	34	M	W	σIII	++++
2153	7	0.4	"	3.7432	0.8370	22.36	0.597	23	M	W	σII	Neg.
2681	5	0.4	"	4.6152	0.9907	21.46	1.20	30	M	B	σII	++++
2641	2	0.4	"	4.8640	1.0081	20.72	2.47	49	M	B	σIII	++++
2632	5	0.4	"	3.3889	0.7075	20.87	2.12	25	M	W	σI	+
2645	3	0.4	10 day	3.9187	0.8863	22.61	2.82	23	M	W	σII	++++
2616	9	0.4	"	5.0031	1.1322	22.62	2.35	40	M	W	σII	++++
2668	44	0.4	2 wk.	4.2733	0.9237	21.61	1.73	45	M	W	σIII	++++
2656	35	0.4	"	6.5613	1.4542	22.16	0.343	29	M	W	σII	++
2173	3	0.4	"	5.4746	1.3562	24.71	1.17	30	M	W	σII	++++
2161	0	0.4	"	4.5260	1.0274	22.69	0.973	36	M	W	σIII	++++
2662	5	0.4	"	5.4100	1.1739	21.69	0.77	23	M	W	σIII	++++
2167	16	0.4	"	4.6141	1.1678	25.30	0.0428	18	M	B	σIII	++++
2690	1	0.4	"	......	1.2154	.....	4.93	?	M	W	Latent	+++
2652	18	0.4	"	3.3117	0.7168	21.64	1.11	25	M	B	σII	++++
2155	0	0.4	"	4.7240	0.9581	20.28	0.0521	35	M	W	σIII	++++
2157	26	0.4	3 wk.	5.0938	1.2487	24.51	0	29	M	W	σII	++
2688	44	0.4	"	4.0904	0.8742	21.37	0.857	33	M	W	σIII	Neg.
2693	12	0.4	"	5.3573	1.1371	21.22	4.10	45	M	W	σIII	+++
2637	0	0.4	"	5.4274	1.2332	22.72	0.751	34	M	W	σIII	++++
2615	7	0.4	"	3.8235	0.8460	22.12	1.41	33	M	W	σIII	++++
2622	7	0.4	1 mo.	5.6000	1.2031	21.48	1.66	38	M	W	σII	++++
2664	67	0.4	"	4.4031	1.0337	23.47	0	42	M	W	σIII	+
2699	13	0.4	"	4.6597	1.0030	21.52	1.99	25	M	W	σIII	++++
2697	3	0.4	"	6.2353	1.3937	22.19	0.215	49	M	W	σIII	++++
2691	44	0.4	5 wk.	3.7374	0.9140	24.45	0	45	M	W	σIII	++++
2620	9	0.4	6 wk.	5.3596	1.1314	21.10	0	31	M	W	σIII	Neg.
2639	13	0.4	2 mo.	5.3934	1.2339	22.87	0.810	23	M	W	σII	++++
2171	5	0.4	"	3.9785	0.9147	23.24	0.218	23	M	B	σII	++
2159	30	0.4	3 mo.	3.2302	0.7573	23.44	0.880	28	M	B	σIII	++++
2629	17	0.4	"	5.5943	1.2485	22.31	0.8009	29	M	W	σIII	Neg.
2151	7	0.4	6 mo.	3.6940	0.7948	21.51	0	27	M	W	σII	++++
2695	13	0.4	7½ mo.	5.0932	1.1871	23.30	0.561	53	M	W	σIII	++++

TABLE IV

The results found in this group comprise a detailed analysis of the values in Table III, showing the percent solids and arsenic content of blood at varying intervals and tabulated according to the classification of the disease.

BLOOD CHART IV

SERIAL NO.	NO. PREV. INJEC.	DOSE OF DRUG	TIME AFTER INJEC.	WT. OF SPECIMEN		PERCENT SOLIDS	AS IN MG. PER 100 GMS. SPEC.	AGE	SEX	COLOR	DIAGNOSIS	WASS.
				MOIST	DRY							
						PRIMARY SYPHILIS						
						Interval—Immediate						
2148	2	0.4	0 +	2.3397	0.5263	22.409	6.33	30	M	W	σI	Neg.
						Interval—5 minutes						
2395	2	0.4	5 min.	3.8865	0.8789	22.62	0.113	22	M	W	σI	Neg.
2396	8	0.4	"	4.8146	1.0360	21.54	1.28	31	M	W	σI	Neg.
						Interval—15 minutes						
2430	0	0.4	15 min.	4.7166	0.9241	19.59	0.270	20	M	B	σI	Neg.
						Interval—24 hours						
2350	9	0.4	24 hr.	4.3968	0.9582	21.79	0.313	30	M	W	σI	Neg.
2192	6	0.3	"	3.6535	0.7320	20.03	0.273	15	F	W	σI	Neg.
						Interval—72 hours						
2575	0	0.4	72 hr.	5.3932	1.2221	22.66	0	38	M	B	σI	Neg.
2313	3	0.4	"	4.2737	0.9109	21.31	0.109	31	M	W	σI	Neg.
2147	1	0.4	"	3.9069	0.9544	24.43	0.209	30	M	W	σI	Neg.
						SECONDARY SYPHILIS						
						Interval—Immediate						
2150	5	0.4	0 +	5.1393	1.0936	21.27	2.91	28	M	W	σII	++++
2623	8	0.4	"	3.8174	0.6838	17.91	21.9	38	M	W	σII	++++
2168	17	0.4	"	4.0161	0.9102	22.66	0.366	18	M	B	σII	++++
2172	6	0.4	"	6.0391	1.4688	24.32	1.02	23	M	B	σII	++

2174	5	0.4	0 +	5.0100	1.0866	21.68	1.83	30	M	W	σII	++++
2176	8	0.4	"	3.0898	0.6406	20.73	0.891	?	M	W	σII	++++
2636	2	0.4	"	3.6687	0.7935	21.08	5.04	20	M	B	σII	++++
2659	1	0.4	"	2.7391	0.5705	20.82	5.84	30	M	W	σII	++++
2653	19	0.4	"	4.0093	0.8438	21.04	5.92	25	M	W	σII	++++
2166	2	0.4	"	2.8745	0.6400	22.26	0.3905	29	M	W	σII	++++
2617	19	0.4	"	5.4092	1.2159	22.47	2.46	40	M	W	σII	++++
2154	8	0.4	"	4.1106	0.9528	23.17	2.62	23	M	W	σII	++++
2152	8	0.4	"	5.1863	1.0351	19.95	2.41	27	M	W	σII	+
2671	10	0.4	"	4.2736	0.9177	21.47	5.44	24	M	W	σII	++++
2682	10	0.4	"	5.9795	1.2850	21.48	7.77	30	M	B	σII	++++
2633	6	0.4	"	4.2410	0.9660	22.77	3.45	25	M	W	σII	+++
Interval—5 minutes												
2400	38	0.4	5 min.	3.8630	0.8140	21.08	0.351	28	M	B	σII	Neg.
2392	3	0.4	"	1.9284	0.4579	23.74	1.45	23	M	B	σII	++
2389	13	0.4	"	3.9594	0.8943	22.58	0	40	M	W	σII	++++
2394	6	0.4	"	4.2590	0.8970	21.06	0.222	27	M	W	σII	++++
2390	25	0.4	"	4.4463	1.0250	23.05	0.195	20	M	W	σII	++++
Interval—10 minutes												
2484	15	0.4	10 min.	3.9878	0.8884	22.27	3.001	22	M	W	σII	Neg.
2404	20	0.4	"	3.7929	0.8496	22.59	0	35	M	W	σII	Neg.
2503	21	0.4	"	4.1097	0.9112	22.17	2.19	27	M	W	σII	Neg.
2403	18	0.4	"	3.9094	0.8165	20.63	3.67	40	F	W	σII	Neg.
2509	3	0.4	"	3.4122	0.7889	23.12	3.80	23	M	W	σII	++++
2506	15	0.4	"	4.5319	0.9915	22.01	1.50	40	M	W	σII	++++
Interval—15 minutes												
2431	11	0.4	15 min.	4.8299	0.9922	20.54	1.61	27	M	W	σII	++++
Interval—20 minutes												
2541	2	0.3	20 min.	4.9275	0.8660	17.57	1.15	35	F	W	σII	++++
SECONDARY SYPHILIS												
Interval—30 minutes												
2489	6	0.4	30 min.	4.0650	0.8968	22.06	0.055	38	M	W	σII	++++

BLOOD CHART IV— Continued

SERIAL NO.	NO. PREV. INJEC.	DOSE OF DRUG	TIME AFTER INJEC.	WT. OF SPECIMEN MOIST	WT. OF SPECIMEN DRY	PERCENT SOLIDS	AS IN MG. PER 100 GMS. SPEC.	AGE	SEX	COLOR	DIAGNOSIS	WASS.
SECONDARY SYPHILIS—Continued												
Interval—30 minutes—Continued												
2505	40	0.4	30 min.	3.8975	0.8750	22.45	0.342	28	M	B	σII	Neg.
2495	0	0.4	"	4.8234	0.9771	20.25	1.53	37	M	B	σII	++++
2510	4	0.4	"	3.1297	0.7201	23.00	0.694	25	M	B	σII	++
2491	4	0.4	"	4.1200	0.8685	20.59	0.345	30	M	B	σII	++++
2486	0	0.4	"	4.4919	0.9930	22.106	0.1007	25	M	W	σII	+++
Interval—24 hours												
2188	0	0.4	24 hr.	3.5624	0.7829	21.97	1.27	36	M	W	σII	++++
Interval—48 hours												
2333	4	0.4	48 hr.	3.9328	0.9185	23.35	2.72	36	M	W	σII	++++
Interval—72 hours												
2572	1	0.4	72 hr.	2.9263	0.6758	22.81	0	37	M	B	σII	++++
2507	0	0.4	"	4.8296	0.9089	18.81	0.366	20	M	W	σII	++++
2149	4	0.4	"	4.1871	0.8336	19.908	0.239	28	M	W	σII	++++
Interval—96 hours												
2324	9	0.4	96 hr.	3.8716	0.7956	20.54	1.67	28	M	W	σII	++++
2331	1	0.4	"	3.6858	0.7678	20.83	1.30	27	M	W	σII	++++
Interval—1 week												
2175	8	0.4	1 wk.	2.1695	0.4711	21.71	0.424	?	M	W	σII	++++
2635	2	0.4	"	4.4885	0.9616	21.42	1.03	20	M	B	σII	++++
2658	0	0.4	"	4.8198	0.9952	20.64	1.205	30	M	W	σII	++++
2165	1	0.4	"	3.9883	0.9672	24.25	0	29	M	W	σII	++++
2153	7	0.4	"	3.7432	0.8370	22.36	0.593	23	M	W	σII	Neg.
2670	9	0.4	"	5.0662	1.2127	23.93	0.206	25	M	W	σII	++++
2681	5	0.4	"	4.6152	0.9907	21.46	1.20	30	M	B	σII	++++
2632	5	0.4	"	3.3889	0.7075	20.87	2.12	25	M	W	σII	+

						Interval—10 days						
2645	3	0.4	10 day	3.9187	0.8863	22.61	2.82	23	M	W	σII	++++
2616	9	0.4	"	5.0031	1.1322	22.62	2.35	40	M	W	σII	++++
						Interval—2 weeks						
2656	35	0.4	2 wk.	6.5613	1.4542	22.16	0.343	29	M	W	σII	++
2173	5	0.4	"	5.4746	1.3562	24.77	1.17	30	M	W	σII	++++
2652	18	0.4	"	3.3117	0.7168	21.64	1.11	25	M	W	σII	++++
						Interval—3 weeks						
2157	26	0.4	3 wk.	5.0938	1.2487	24.51	0	29	M	W	σII	++
						Interval—1 month						
2622	7	0.4	1 mo.	5.6000	1.2031	21.48	1.66	38	M	W	σII	++++
						Interval—2 months						
2171	5	0.4	2 mo.	3.9785	0.9147	23.25	0.218	23	M	B	σII	++
2639	13	0.4	"	5.3934	1.2339	22.89	0.810	23	M	W	σII	++++
						Interval—6 months						
2151	8	0.4	6 mo.	3.6940	0.7948	21.51	0	27	M	W	σII	++++
						TERTIARY SYPHILIS						
						Interval—Immediate						
2655	1	0.4	0 +	3.3287	0.7357	22.10	5.60	39	M	W	σIII	Neg.
2669	52	0.4	"	4.5900	0.9517	20.73	2.10	40	M	W	σIII	++++
2694	13	0.4	"	4.7921	0.9969	20.80	1.003	45	M	W	σIII	+++
2687	45	0.4	"	4.1605	0.9155	22.04	2.18	33	M	W	σIII	Neg.
2625	3	0.4	"	4.9020	0.9003	18.37	2.96	41	M	W	σIII	+++
2661	15	0.4	"	3.2521	0.6236	19.17	0.801	34	M	W	σIII	++++
2158	28	0.4	"	5.6377	1.3450	23.86	1.85	30	M	W	σIII	++++
2657	32	0.4	"	5.5928	1.1417	20.41	7.007	30	M	W	σIII	++++
2692	45	0.4	"	5.1711	1.2514	22.07	1.99	45	M	W	σIII	++++
2170	3	0.4	"	5.6101	1.2215	21.77	3.68	23	M	W	σIII	+++

Blood Chart IV—Continued

SERIAL NO.	NO. PREV. INJEC.	DOSE OF DRUG	TIME AFTER INJEC.	WT. OF SPECIMEN		PERCENT SOLIDS	AS IN MG. PER 100 GMS. SPEC.	AGE	SEX	COLOR	DIAGNOSIS	WASS.
				MOIST	DRY							
					TERTIARY SYPHILIS—Continued							
					Interval—Immediate—Continued							
2640	14	0.4	0 +	6.6982	1.4665	21.89	4.09	23	M	W	σIII	++++
2164	1	0.4	ʻʻ	2.6259	0.5308	20.21	0.289	37	M	W	σIII	++++
2160	31	0.4	ʻʻ	3.3800	0.7050	20.85	3.54	28	M	B	σIII	++++
2162	2	0.4	ʻʻ	5.9649	1.3579	22.79	1.76	36	M	W	σIII	++++
2667	9	0.4	ʻʻ	4.3226	0.8929	20.65	2.79	26	M	W	σIII	++++
2696	14	0.4	ʻʻ	5.0196	1.1713	23.33	1.49	53	M	W	σIII	++++
2156	1	0.4	ʻʻ	3.4133	0.7020	20.56	5.69	35	M	B	σIII	++++
2684	50	0.4	ʻʻ	4.1825	0.8934	21.36	2.23	27	M	W	σIII	+++
2665	68	0.4	ʻʻ	4.6634	1.0506	22.52	5.71	42	M	W	σIII	Neg.
2651	29	0.4	ʻʻ	3.1359	0.6544	20.54	6.11	42	M	B	σIII	+
2631	0	0.3	ʻʻ	4.5829	1.0167	22.18	4.91	43	M	W	σIII	++++
2700	14	0.4	ʻʻ	4.1364	0.8365	20.87	11.5	25	M	W	σIII	++++
2618	6	0.4	ʻʻ	5.0372	0.9940	19.70	4.02	54	M	W	σIII	++++
2686	2	0.4	ʻʻ	5.4680	1.2034	22.19	16.6	34	M	W	σIII	+
2628	18	0.3	ʻʻ	5.5794	1.2950	23.21	1.54	29	M	W	σIII	+
2638	1	0.4	ʻʻ	5.3865	1.1601	21.53	4.30	34	M	W	σIII	++++
2698	4	0.4	ʻʻ	4.7282	1.0538	22.28	0.948	49	M	W	σIII	++++
2614	8	0.4	ʻʻ	5.7946	1.3271	22.90	7.53	33	M	W	σIII	++++
2642	3	0.4	ʻʻ	5.0682	0.9430	18.60	5.30	49	M	B	σIII	++++
2663	6	0.4	ʻʻ	4.5641	0.8870	19.43	6.70	23	M	W	σIII	++++
2644	1	0.4	ʻʻ	4.7885	1.0496	21.91	1.90	22	M	B	σIII	Neg.
2689	2	0.4	ʻʻ	4.6314	1.0409	22.47	5.76		M	W	Latent	+++
					Interval—5 minutes							
2393	14	0.4	5 min.	5.2987	1.1316	21.33	0.265	45	M	W	σIII	++++
2399	4	0.4	ʻʻ	4.3645	0.9695	22.21	1.54	32	M	W	σIII	++++
2387	13	0.4	ʻʻ	4.3340	0.9405	21.70	0.850	33	M	W	σIII	++++
2398	3	0.3	ʻʻ	1.0162	0.2198	21.63	1.51	45	M	W	σIII	++

2391	20	0.4	5 min.	4.6547	1.0734	23.08	1.47	35	M	B	σIII	++
2397	13	0.3	"	4.9715	0.9801	19.72	5.101	26	F	W	σIII	++
2386	14	0.3	"	3.0540	0.6624	21.68	5.28	20	F	W	σIII	+++
Interval—10 minutes												
2408	4	0.4	10 min.	2.8255	0.6218	22.01	0	56	M	B	σIII	++++
2492	7	0.4	"	4.3140	0.9617	22.29	0	30	M	B	σIII	++++
2405	3	0.3	"	......	0.5759	.....	0.173		F	W	σIII	++++
2485	14	0.4	"	4.5045	1.0275	22.81	0.583	24	M	W	σIII	+
2407	11	0.4	"	2.7768	0.5981	21.53	0.167	38	M	W	σIII	++++
2402	1	0.3	"	4.0135	0.8335	20.76	0.599	21	F	W	σIII	++++
2501	3	0.4	"	5.0434	1.1076	21.96	0.902	49	M	W	σIII	++++
2409	11	0.3	"	3.9604	0.7824	19.76	0.255		F	B	Latent	Neg.
Interval—15 minutes												
2488	9	0.4	15 min.	4.6543	0.9114	19.58	0.2190	41	M	W	σIII	++++
2502	3	0.4	"	3.0015	0.6630	22.08	3.77	43	M	B	σIII	++++
2429	6	0.4	"	4.7856	0.9728	20.32	0.102	56	M	B	σIII	++++
2411	4	0.4	"	4.7540	1.0583	22.26	0.094	32	M	B	σIII	+
2412	3	0.4	"	5.9600	1.4259	23.92	0.526	34	M	W	σIII	++++
2435	11	0.3	"	5.2400	1.1278	21.52	0.086	27	F	W	σIII	++++
2547	5	0.4	"	4.8095	1.0192	21.19	0.588	24	M	W	σIII	++++
2504	14	0.4	"	4.1295	0.8438	20.43	3.15	32	M	B	σIII	++
2433	8	0.4	"	4.7238	0.9746	20.63	0	22	M	W	σIII	++++
2543	1	0.4	"	5.5583	1.2088	21.74	0.827	50	M	B	σIII	++++
2413	2	0.4	"	3.9212	0.8956	22.84	3.72	49	M	W	σIII	Neg.
Interval—20 minutes												
2438	2	0.2	20 min.	5.5429	1.0704	19.31	0.4607	36	F	B	σIII	+++
2548	7	0.2	"	3.8702	0.8059	20.79	0	46	F	B	σIII	++++
2442	0	0.3	"	4.2692	0.9592	22.46	0.208	27	F	W	σIII	++++
2428	11	0.3	"	4.8415	1.0305	21.28	1.94	35	F	W	σIII	++++
2440	1	0.3	"	4.6932	0.9476	20.19	0.105	30	F	B	σIII	++
2446	10	0.3	"	4.5666	0.9541	20.89	1.57	51	F	W	σIII	++++
2437	0	0.3	"	5.0569	1.0708	21.17	0.186	39	F	W	σIII	++++
2447	2	0.3	"	5.0052	1.0156	20.29	0.098	29	F	W	σIII	++++

BLOOD CHART IV— Continued

SERIAL NO.	NO. PREV. INJEC.	DOSE OF DRUG	TIME AFTER INJEC.	WT. OF SPECIMEN		PERCENT SOLIDS	AS IN MG. PER 100 GMS. SPEC.	AGE	SEX	COLOR	DIAGNOSIS	WASS.
				MOIST	DRY							
TERTIARY SYPHILIS—Continued												
Interval—20 minutes—Continued												
2445	0	0.2	20 min.	4.4766	0.9062	20.24	0.220	19	F	B	σIII	++++
2441	3	0.2	″	5.6544	1.1267	19.92	0.266	30	F	B	σIII	+++
2542	7	0.3	″	4.8327	1.0027	21.16	1.46	33	M	W	σIII	++++
2545	1	0.3	″	4.8861	1.0130	20.73	0.658	39	F	W	σIII	++++
2544	1	0.4	″	4.8456	0.8552	17.66	3.50	23	M	B	σIII	++++
Interval—30 minutes												
2487	56	0.4	30 min.	4.6136	1.0427	22.60	0.767	28	M	W	σIII	++++
2444	3	0.4	″	4.2202	0.9102	21.56	0	?	M	B	σIII	++++
2546	9	0.3	″	5.0021	0.9620	19.23	2.59	27	F	W	σIII	++++
2508	14	0.4	″	3.6134	0.8034	22.23	1.55	37	M	B	σIII	++++
2434	53	0.4	″	3.3079	0.7694	23.26	0	40	M	W	σIII	Neg.
2443	0	0.3	″	4.1226	0.8142	19.74	0.122		M	W	Latent	Neg.
Interval—1 hour												
2311	0	0.3	1 hr.	7.0768	1.5022	21.22	0	55	F	W	σIII	++++
2603	2	0.3	″	5.9335	1.1471	19.34	Trace	30	F	W	σIII	++++
2602	13	0.4	″	4.6688	0.9903	21.21	0.252	43	M	W	σIII	++++
2597	22	0.3	″	7.1950	1.4590	20.27	0.685	40	F	W	σIII	+++
2594	0	0.3	″	5.4069	1.0999	20.34	1.81	33	F	B	σIII	++++
2312	3	0.3	″	5.3730	1.0265	19.10	Trace	25	F	B	σIII	++++
2593	16	0.3	″	4.5558	1.0068	22.09	0.331	34	F	W	σIII	++++
2598	13	0.3	″	4.6845	1.0000	21.34	0.20	38	F	W	σIII	++++
2596	10	0.3	″	5.6179	1.1881	21.14	0.841	51	F	W	σIII	++++
2490	14	0.4	″	3.9496	0.9384	23.75	0.106	37	M	B	σIII	++++
2309	1	0.3	″	4.9211	0.9198	18.69	0.434	24	F	B	σIII	++++
2601	1	0.4	″	5.6296	1.2603	22.45	0.988	22	M	B	σIII	Neg.
2599	2	0.4	″	7.3056	1.5361	21.02	0.13		M	W	Latent	++++

2600	13	0.4	1 hr.	6.4102	1.4557	22.70	0.681		M	W	Latent	Neg.
2595	4	0.4	"	8.1402	1.7480	21.47	1.14		M	B	Latent	++++
2521	9	0.4	"		0.7295		1.02	36	M	W	Latent	++++
						Interval—2 hours						
2329	2	0.3	2 hr.	4.3720	0.6603	15.10	0.454		F	W	σIII	++++
2310	21	0.4	"	4.3928	0.9073	20.63	0	42	M	W	σIII	+
						Interval—24 hours						
2248	10	0.3	24 hr.	3.9950	0.9178	22.97	0	28	F	B	σIII	Neg.
2241	0	0.4	"	4.2419	0.9457	22.29	1.32	43	M	B	σIII	++++
2374	12	0.4	"	4.9899	1.1969	23.98	0.167	32	M	W	σIII	Neg.
2187	31	0.4	"	4.1090	0.9537	23.21	0.052	28	M	B	σIII	++++
2376	0	0.3	"	3.5988	0.8196	22.77	0.488	30	M	B	σIII	Neg.
2414	1	0.4	"	4.5919	1.0784	23.48	0	40	M	B	σIII	Neg.
2247	1	0.3	"	3.9596	0.8444	21.32	0.355	25	F	B	σIII	++++
2452	1	0.4	"	4.2695	1.0269	24.05	0.194	20	M	W	Latent	++++
2191	5	0.4	"	3.7930	0.8430	21.98	0.0593		M	W	Latent	++++
2278	9	0.4	"	3.1472	0.7237	22.99	0	29	M	W	Latent	Neg.
						Interval—48 hours						
2242	0	0.4	48 hr.	3.9105	0.8638	22.08	0.463	40	M	B	σIII	++++
2330	12	0.4	"	5.3253	1.2069	22.66	0.331	26	M	W	σIII	++++
2375	12	0.4	"	4.3885	0.9858	22.46	0.101	32	M	W	σIII	Neg.
2246	3	0.4	"	4.7892	1.0539	22.005	Trace	21	M	B	σIII	++++
2238	7	0.4	"	3.1510	0.6269	19.89	0.0797	35	M	B	σIII	++++
2288	0	0.4	"	6.9265	1.6049	23.17	0.187	54	M	W	σIII	++++
2415	1	0.4	"	4.6346	1.1490	24.78	1.39	40	M	B	σIII	Neg.
2289	2	0.4	"	6.9819	1.5779	22.59	0.383	44	M	B	σIII	++++
2327	10-15	0.4	"	4.9505	1.0713	21.64	0.932	37	M	W	σIII	Neg.
2286	8	0.3	"	5.8200	1.2083	20.42	0.0413		M	W	Latent	+
2282	?	0.4	"	1.7931	0.3881	21.64	1.03		F	W	Latent	++++
2453	1	0.4	"	4.4223	0.9930	22.45	1.006	20	M	W	Latent	++++
2279	9	0.4	"	4.0509	0.8950	22.09	0	29	M	W	Latent	Neg.

BLOOD CHART IV— Continued

SERIAL NO.	NO. PREV. INJEC.	DOSE OF DRUG	TIME AFTER INJEC.	WT. OF SPECIMEN		PERCENT SOLIDS	AS IN MG. PER 100 GMS. SPEC.	AGE	SEX	COLOR	DIAGNOSIS	WASS.
				MOIST	DRY							
						TERTIARY SYPHILIS—Continued						
						Interval—72 hours						
2243	0	0.4	72 hr.	4.9344	1.0934	22.15	1.21	43	M	B	σIII	++++
2570	6	0.3	"	4.9321	1.0140	20.56	0	22	F	W	σIII	++++
2573	11	0.3	"	5.1727	1.1131	21.51	0.179	35	F	W	σIII	++++
2377	0	0.3	"	4.3300	0.9328	21.54	0.857	30	M	B	σIII	Neg.
2328	10-15	0.4	"	3.8255	0.8780	22.95	1.13	37	M	W	σIII	Neg.
2571	40	0.3	"	6.3780	1.3738	21.54	0.036	38	F	W	σIII	++++
2287	8	0.3	"	3.8418	0.8250	20.47	0.484		M	W	Latent	+
2315	4	0.4	"	4.9940	1.1076	22.17	1.80	54	M	W	Latent	++++
2283		0.4	"	3.6424	0.7748	21.27	0		F	W	Latent	++++
2547	20	0.3	"	4.9267	0.9356	18.99	0.23	28	F	B	Latent	++++
						Interval—96 hours						
2325	2	0.3	96 hr.	2.9770	0.6440	21.62	0.310	32	M	W	σIII	++++
2195	0	0.3	"	3.6123	0.7900	21.86	0.126	32	M	W	σIII	++++
2525	5	0.3	"	3.9005	0.8154	20.90	1.83	34	M	W	σIII	++++
2237	2	0.3	"	5.5441	1.1725	22.24	0	36	M	W	σIII	++++
2197	40	0.3	"	3.9443	0.8368	21.21	0	49	F	W	σIII	++++
2332	20	0.3	"	5.2686	1.1465	21.76	0.0871	49	M	W	σIII	++++
2194	2	0.3	"	4.8391	1.1811	24.61	0.169	34	M	W	σIII	++++
2193	9	0.3	"	4.1680	0.9358	22.45	0	22	M	W	σIII	++++
2196	0	0.3	"	4.1503	0.8708	20.98	1.14		F	W	Latent	++++
2524	21	0.4	"	5.7924	1.1655	20.12	0.343	42	M	W	Latent	+
						Interval—5 days						
2654	0	0.4	5 day	2.9021	0.6631	22.84	2.41	39	M	W	σIII	Neg.
2660	14	0.4	"	3.7574	0.7553	20.70	0.264	34	M	W	σIII	++++
2666	8	0.4	"	4.3480	0.9123	20.98	0	26	M	W	σIII	++++
2643	0	0.4	"	3.7444	0.8000	21.36	0.750	22	M	B	σIII	Neg.

Interval—1 week													
2169	2		0.4	1 wk.	3.4027	0.7489	22.008	0.133	23	M	W	σIII	+++
2163	0		0.4	"	4.9726	1.1623	23.37	1.14	37	M	W	σIII	+++
2634	3		0.3	"	5.7875	1.2948	22.37	0.386	47	M	W	σIII	++++
2683	49		0.4	"	5.6911	1.2382	21.75	0.161	27	M	W	σIII	+++
2650	28		0.4	"	3.8474	0.8971	23.31	1.11	42	M	B	σIII	+
2685	1		0.4	"	5.0507	1.1249	22.27	4.14	34	M	W	σIII	++++
2619	5	2neo 3SS	0.4	"	6.4963	1.2887	19.83	0.931	54	M	W	Latent	++++
2641	2		0.4	"	4.8640	1.0081	20.72	2.47	49	M	B	σIII	++++
Interval—2 weeks													
2668	44		0.4	2 wk.	4.2733	0.9237	21.61	1.73	45	M	W	σIII	++++
2161	0		0.4	"	4.5260	1.1274	22.69	0.973	36	M	W	σIII	++++
2662	5		0.4	"	5.4100	1.1738	21.69	0.77	23	M	W	σIII	++++
2167	16		0.4	"	4.6141	1.1678	25.30	0.0428	18	M	B	σIII	++++
2155	0		0.4	"	4.7240	0.9581	20.28	0.0531	35	M	B	σIII	++++
Interval—3 weeks													
2688	44		0.4	3 wk.	4.0904	0.8742	21.37	0.857	33	M	W	σIII	Neg.
2693	12		0.4	"	5.3573	1.1371	21.22	4.10	45	M	W	σIII	+++
2637	0		0.4	"	5.4274	1.2332	22.72	0.751	34	M	W	σIII	+
2615	7		0.4	"	3.8235	0.8460	22.12	1.41	33	M	W	σIII	++++
Interval—1 month													
2664	67		0.4	1 mo.	4.4031	1.0337	23.47	0	42	M	W	σIII	+
2699	13		0.4	"	4.6597	1.0030	21.52	1.99	25	M	W	σIII	++++
2697	3		0.4	"	6.2353	1.3937	22.19	0.215	49	M	W	σIII	+
Interval—5 weeks													
2691	44		0.4	5 wk.	3.7374	0.9140	24.45	0	45	M	W	σIII	++++
Interval—6 weeks													
2620	9		0.4	6 wk.	5.3596	1.1314	21.10	0	31	M	W	σIII	Neg.

BLOOD CHART IV— Continued

SERIAL NO.	NO. PREV. INJEC.	DOSE OF DRUG	TIME AFTER INJEC.	WT. OF SPECIMEN MOIST	WT. OF SPECIMEN DRY	PERCENT SOLIDS	AS IN MG. PER 100 GMS. SPEC.	AGE	SEX	COLOR	DIAGNOSIS	WASS.
						TERTIARY SYPHILIS—Continued						
						Interval—3 months						
2159	30	0.4	3 mo.	3.2312	0.7573	23.44	0.88	28	M	B	σIII	++++
2629	17	0.4	"	5.5943	1.2485	22.31	0.8009	29	M	W	σIII	+
						Interval—7½ months						
2695	13	0.4	7½ mo.	5.0932	1.1871	23.30	0.561	53	M	W	σIII	++++
						CONGENITAL SYPHILIS						
						Interval—Immediate						
2627	13	0.4	0 +	4.7223	1.0665	22.58	1.40	20	M	W	Cong.	++++
						Interval—10 minutes						
2406	5	0.4	10 min.	3.6288	0.7460	20.56	0.066	17	M	W	Cong.	+++
2401	6	0.3	"	3.5505	0.6373	18.00	0	25	F	B	Cong.	++++
2410	2	0.3	"	4.2334	0.9027	21.32	0.0553	22	F	W	Cong.	+++
						Interval—20 minutes						
2439	16	0.3	20 min.	6.8300	1.3139	19.23	0.076	19	F	B	Cong.	++++
						Interval—24 hours						
2189	2	0.3	24 hr.	3.7317	0.7187	19.25	0.139	22	F	W	Cong.	++++
2190	0	0.4	"	3.0162	0.60826	22.63	0.293	17	M	W	Cong.	++++
						Interval—48 hours						
2245	8	0.25	48 hr.	3.8874	0.9175	23.601	0.435	15	M	W	Cong.	++++
						Interval—96 hours						
2522	7.	0.3	96 hr.	5.3332	1.0639	19.94	0.234	17	M	W	Cong.	++++

						Interval—1 week					
2649	7	0.3	1 wk.	4.5471	0.9818	21.59	0.305	15	M	W	Cong.	++++
2626	12	0.4	"	5.5464	1.2645	22.79	0.988	20	M	W	Cong.	++++
						NON-SYPHILITIC						
						Interval—24 hours						
2239	0	0.4	24 hr.	4.0568	0.9067	22.36	0.367		M	W	Nonsyph.	Neg.
2416	0	0.4	"	4.8467	0.9762	20.14	0.409	15	M	W	Nonsyph.	Neg.
						Interval—48 hours						
2417	0	0.4	48 hr.	4.7091	1.0506	22.31	0.438	15	M	W	Nonsyph.	Neg.
2240	0	0.4	"	3.9144	0.7659	19.56	0.0652		M	W	Nonsyph.	Neg.
						Interval—72 hours						
2280	0	0.4	72 hr.	5.4121	1.2051	22.26	0.995	29	M	W	Nonsyph.	Neg.
						Interval—96 hours						
2523	0	0.4	96 hr.	5.2517	1.0405	19.81	0.0961	25	F	W	Nonsyph.	Neg.
2244	0	0.4	"	5.1086	1.1168	21.07	0	34	M	W	Nonsyph.	Neg.

Detailed Analyses of Tables III and IV, Giving the Number of Cases in the Group with the Wassermann, Dose of Drug, and Number of Previous Injections Together with the Highest Arsenic Value, the Lowest Arsenic Value, and the Average Amount Found in This Group.

INTERVAL—IMMEDIATE

PRIMARY SYPHILIS: 1 case; Wassermann negative.

Amount of arsenic: 6.33 mg. after 0.4 gm. and 2 previous injections at 3 and 4 day intervals; male, white, aged 30.

SECONDARY SYPHILIS: 16 cases; Wassermann positive.

No. of previous injections: 1–19.

Dose: 0.4 gm.

Smallest amount of arsenic: 0.366 mg. after 0.4 gm. and 17 previous injections, irregularly at 2 week intervals, this being the 4th injection in the new course; male, black, aged 18.

Largest amount of arsenic: 21.9 mg. after 0.4 gm. and 8 previous injections at 2 and 4 day intervals; male, white, aged 38.

Average amount of arsenic in this group: 4.39 mg.

TERTIARY SYPHILIS: 32 cases; 28 with positive Wassermann; 4 negative Wassermann.

No. of previous injections: 1–68.

Dose: 0.3 gm. 2 cases; 0.4 gm. 30.

Smallest amount of arsenic: 0.289 mg. after 0.4 gm. and 1 previous injection the week before; male, white, aged 37.

Largest amount of arsenic: 16.6 mg. after 0.4 gm. and 1 previous injection the week before; male, white, aged 34.

Average amount of arsenic in this group: 4.18 mg.

CONGENITAL SYPHILIS: 1 case.

Amount of arsenic: 1.40 mg. after 0.4 gm. and 13 previous injections, last being 4th of second course after 5 months' rest; male, white, aged 20.

INTERVAL—5 MINUTES

PRIMARY SYPHILIS: 2 cases; Wassermann negative.

No. of previous injections: 2–8.

Smaller amount of arsenic: 0.113 mg. following 0.4 gm. and 1 previous injection a week before; male, white, aged 22.

Larger amount of arsenic: 1.28 mg. following 0.4 gm. and 8 previous injections at 2–4 day intervals; male, white, aged 31.

Average amount of arsenic in this group: 0.7 mg.

SECONDARY SYPHILIS: 5 cases; 4 with positive Wassermann, 1 with negative.

No. of previous injections: 3–38.

Dose: 0.4 gm.

Smallest amount of arsenic: 0 after 0.4 gm. and 13 previous injections, this being the 4th of a second course after 2 months' rest; male, white, aged 40.

Largest amount of arsenic: 1.45 mg. after 0.4 gm. and three previous injections; none for 6 weeks; male, black, aged 23.

Average amount of arsenic in this group: 0.44 mg.

TERTIARY SYPHILIS: 7 cases; Wassermann positive.

No. of previous injections: 3–20.

Dose: 0.3 gm., 2 cases; 0.4 gm., 5 cases.

Smallest amount of arsenic: 0.265 mg. following 0.4 gm. and 14 previous injections; last 11 months ago; male, white, aged 45.

Largest amount of arsenic: 5.28 mg. after 0.3 gm. and 14 previous injections; last course irregular; no treatment for a month; female, white, aged 20.

Average amount of arsenic in this group: 2.29 mg.

INTERVAL—10 MINUTES

SECONDARY SYPHILIS: 6 cases; 2 with positive Wassermann; 4 with negative Wassermann.

No. of previous injections: 3–21.

Dose: 0.3 gm. 1 case; 0.4 gm. 5 cases.

Smallest amount of arsenic: 0 after 0.4 gm. and 20 previous injections; male, white, aged 35.

Largest amount of arsenic: 3.80 mg. after 0 gm. and 3 previous injections weekly; male; white; aged 23.

Average amount of arsenic in this group: 2.36 mg.

TERTIARY SYPHILIS: 8 cases; 7 Wassermann positive, 1 negative.

No. of previous injections: 1-14.

Dose: 0.3 gm. 3 cases; 0.4 gm., 5 cases.

Smallest amount of arsenic: 0 in 2 cases, one male, black, aged 56 had 0.4 gm. and 4 previous injections at 3-4 day intervals; the other male, black, aged 30, had 0.4 gm. and 7 previous injections at irregular intervals.

Largest amount of arsenic: 0.902 mg. after 0.4 gm. and 3 previous injections at 2 week intervals, male, white, aged 49.

Average amount of arsenic in this group: 0.34 mg.

CONGENITAL SYPHILIS: 3 cases; Wassermann positive.

No. of previous injections: 2-6.

Dose: 0.3 gm. 2 cases; 0.4 gm. 1 case.

Smallest amount of arsenic: 0 after 0.3 gm. and 6 previous injections, at intervals of 9 days to a month or more, female, black, aged 25.

Largest amount of arsenic: 0.066 mg. after 0.4 gm. and 5 previous weekly injections, male, white, aged 17.

Average amount of arsenic in this group: 0.04 mg.

INTERVAL—15 MINUTES

PRIMARY SYPHILIS: 1 case; Wassermann negative.

Amount of arsenic: 0.270 mg. following 0.4 gm.; no previous injections; male, black, aged 20.

SECONDARY SYPHILIS: 1 case; Wassermann positive.

Amount of arsenic: 1.61 mg. after 0.4 gm. and 11 previous injections, this being the 5th of a second course; male, white, aged 27.

TERTIARY SYPHILIS: 11 cases; Wassermann positive in 10; negative in 1.

No. of previous injections: 1-9.

Dose: 0.3 gm. 1 case; 0.4 gm. 10 cases.

Smallest amount of arsenic: 0 after 0.4 gm. and 8 previous injections 6 months before, male, white, aged 22.

Largest amount of arsenic: 3.77 mg. after 0.4 gm. and 3 previous injections, 3 weeks before, male, black, aged 43.

Average amount of arsenic in this group: 1.19 mg.

INTERVAL—20 MINUTES

SECONDARY SYPHILIS: 1 case; Wassermann positive.

Amount of arsenic: 1.15 following 0.3 gm. and 2 previous injections, female, white, aged 35.

TERTIARY SYPHILIS: 13 cases; Wassermann positive.

No. of previous injections: 0–11.

Dose: 0.2 gm. in 4 cases; 0.3 gm. 8 cases and 0.4 gm. 1 case.

Smallest amount of arsenic: 0 after 0.2 gm. and 7 previous injections weekly of 0.3 gm.; female, black, aged 46.

Largest amount of arsenic: 3.50 mg. after 0.4 gm. and one previous injection a week before, male, black, aged 23.

Average amount of arsenic in this group: 0.82 mg.

CONGENITAL SYPHILIS: 1 case; Wassermann positive.

Amount of arsenic: 0.076 mg. after 0.3 gm. and 16 previous injections at monthly intervals; female, black, aged 19.

INTERVAL—30 MINUTES

SECONDARY SYPHILIS: 6 cases; Wassermann positive in 5; negative in 1.

No. of previous injections 0–42.

Dose: 0.4 gm.

Smallest amount of arsenic: 0.055 mg. after 0.4 gm. and 6 previous injections at 3–4 day intervals; male, white, aged 38.

Largest amount of arsenic: 1.53 mg. after 0.4 gm.; no previous injections; male, black, aged 37.

Average amount of arsenic in this group: 0.51 mg.

TERTIARY SYPHILIS: 5 cases; Wassermann positive in 4; negative in 1.

Dose: 0.3 gm. in 1 case; 0.4 gm. 4 cases.

No. of previous injections: 3–56.

Smallest amount of arsenic: 0 in 2 patients; one, adult male, black, after 0.4 gm. and 3 previous injections seven months ago; the other, male, white, aged 40, after 0.4 gm. and 53 previous injections, the last 3 months ago.

Largest amount of arsenic: 2.59 mg. after 0.3 gm. and 9 previous injections 3 months ago; female, white, aged 27.

Average amount of arsenic in this group: 0.98 mg.

NONSYPHILITIC: 1 case, Wassermann negative.

Amount of arsenic: 0.122 mg. after 0.3 gm., no previous injections, adult male, white.

INTERVAL—1 HOUR

TERTIARY SYPHILIS: 12 cases; Wassermann positive in 11; negative in 1.

No. of previous injections: 0–22.

Dose: 0.3 gm. 9 cases; 0.4 gm. 3 cases.

Smallest amount of arsenic: 0 after 0.3 gm., no previous injections; female, white, aged 55.

Largest amount of arsenic: 1.81 mg. after 0.3 gm., no previous injections; female, black, aged 33.

Average amount of arsenic: 0.47 mg.

LATENT SYPHILIS: 4 cases; Wassermann positive in 3; negative in 1.

Previous number of injections: 2–9.

Dose: 0.4 gm.

Smallest amount of arsenic: 0.13 mg. after 0.4 gm. and 2 previous weekly injections; adult male, white.

Largest amount of arsenic: 1.14 mg. after 0.4 gm. and 4 previous weekly injections; adult male, black.

Average amount of arsenic: 0.74 mg.

INTERVAL—2 HOURS

TERTIARY SYPHILIS: 2 cases; Wassermann positive.

Larger amount of arsenic: 0.454 mg. after 0.3 gm. and 2 previous injections, at 2 week intervals; adult female, white.

Smaller amount of arsenic: 0 after 0.4 gm. and 21 previous injections, third at weekly intervals after 4 months' rest; male, white, aged 42.

Average amount of arsenic for this group: 0.23 mg.

INTERVAL—24 HOURS

PRIMARY SYPHILIS: 2 cases; Wassermann negative.

Smaller amount of arsenic: 0.273 mg. following 0.3 gm. and 6 previous injections at 3–4 day intervals; female, white, aged 15.

Larger amount of arsenic: 0.313 mg. after 0.4 gm. and 9 previous injections, at 3-5 day intervals; male, white, aged 30.

Average amount of arsenic: 0.29 mg.

SECONDARY SYPHILIS: 1 case; Wassermann positive.

Amount of arsenic: 1.27 mg. after 0.4 gm., no previous injections; male, white, age 36.

TERTIARY SYPHILIS: 7 cases; 4 with negative Wassermann and 3 with positive Wassermann.

No. of previous injections: 0–31.

Dose: 0.3 gm. 3 cases; 0.4 gm. 4 cases.

Smallest amount of arsenic: 0 in two cases; one, female black, aged 28, after 0.3 gm. and 10 previous injections at irregular intervals; the other, male, black, aged 40 after 0.4 gm. and 1 previous injection.

Largest amount of arsenic: 1.32 mg. after 0.4 gm. and no previous injections; male, black, aged 43.

Average amount of arsenic in this group: 0.34 gm.

LATENT SYPHILIS: 3 cases; 1 with negative Wassermann; 2 with positive Wassermann.

No. of previous injections: 1-9.

Dose: 0.4 gm.

Smallest amount of arsenic: 0 after 0.4 gm. and 9 injections 1 year previously; male, white, aged 29.

Largest amount of arsenic: 0.194 mg. after 0.4 gm.; no arsenical treatment for a year; male, white, aged 20.

Average amount of arsenic in this group: 0.127 mg.

NONSYPHILITIC CASES: 2; Wassermann negative.

Smaller amount of arsenic: 0.367 mg. after 0.4 gm., no previous injections; adult male, white.

Larger amount of arsenic: 0.407 mg. after 0.4 gm., no previous injections; male, white, aged 15.

Average amount of arsenic in this group: 0.39 mg.

INTERVAL—48 HOURS

SECONDARY SYPHILIS: 1 case, Wassermann positive.

Amount of arsenic: 2.72 mg. after 0.4 gm. and 4 previous injections at 2 day intervals, then a rest of 2 weeks; male, white, aged 36.

TERTIARY SYPHILIS: 9 cases; 3 with negative Wassermann, 6 with positive.

No. of previous injections: 0–15.

Dose: 0.4 gm.

Smallest amount of arsenic: trace after 0.4 gm. and 1 previous injection a week before; male, black, aged 21.

Largest amount of arsenic: 1.39 mg. after 0.4 gm. and 1 previous injection about a year ago; male, black, aged 40.

Average amount of arsenic in this group: 0.78 mg.

LATENT SYPHILIS: 4 cases; 1 Wassermann negative; 3 Wassermann positive.

No. of previous injections: 1–9.

Dose: 1 case 0.3 gm.; 3 cases 0.4 gm.

Smallest amount of arsenic: 0 after 0.4 gm. and 9 previous injections 1 year ago; male, white, aged 29.

Largest amount of arsenic: 1.03 mg. after 0.4 gm.; no treatment for 7 years; male, white, aged 20.

Average amount of arsenic in this group: 0.52 mg.

CONGENITAL SYPHILIS: 1 case; Wassermann reaction positive.

Amount of arsenic: 0.435 mg. after 0.25 gm. and 8 previous injections several months before; male, white, aged 15.

NONSYPHILITIC: 2 cases; Wassermann negative.

Larger amount of arsenic: 0.438 mg. after 0.4 gm. and 1 previous injection; male, white, aged 15.

Smaller amount of arsenic: 0.0652 mg. after 0.4 gm., no previous treatment, adult male, white.

Average amount of arsenic: 0.25 mg.

INTERVAL—72 HOURS

PRIMARY SYPHILIS: 3 cases; Wassermann negative.

No. of previous injections: 0-3.

Dose: 0.4 gm.

Smallest amount of arsenic: 0 after 0.4 gm.; no previous injections; male, black, aged 38.

Largest amount of arsenic: 0.209 mg. after 0.4 gm. and 1 previous injection, male, white, aged 30.

Average amount of arsenic in this group: 0.11 mg.

SECONDARY SYPHILIS: 3 cases; Wassermann positive.

Smallest amount of arsenic: 0 after 0.4 gm. and 1 previous injection; male, black, aged 37.

Largest amount of arsenic: 0.366 mg. after 0.4 gm. and no previous treatment; male, white, aged 20.

Average amount of arsenic in this group: 0.20 mg.

TERTIARY SYPHILIS: 6 cases; 2 with negative Wassermann; 4 with positive Wassermann.

No. of previous injections: 0–40.

Dose: 0.3 gm., 4 cases; 0.4 gm., 2 cases.

Smallest amount of arsenic: 0 after 0.3 gm. and 6 previous injections at weekly intervals; female, white, aged 22.

Largest amount of arsenic: 1.21 mg. after 0.4 gm., no previous injections; male, black, aged 43.

Average amount of arsenic in this group: 0.57 mg.

LATENT SYPHILIS: 4 cases; Wassermann positive.

No. of previous injections: 0-9.

Dose: 0.3 gm., 1 case; 0.4 gm., 3 cases.

Smallest amount of arsenic: 0 after 0.4 gm., no previous injections; adult female, white.

Largest amount of arsenic: 1.80 mg. after 0.4 gm. and 4 previous weekly injections; male, white, aged 54.

Average amount of arsenic in this group: 0.63 mg.

INTERVAL—96 HOURS

SECONDARY SYPHILIS: 2 cases; Wassermann positive.

Smaller amount of arsenic: 1.30 mg. after 0.4 gm. and 1 previous injection 3 days before; male, white, aged 27.

Larger amount of arsenic: 1.67 mg. after 0.4 gm. and 9 previous injections at 3 to 4 day intervals; male, white, aged 28.

Average amount of arsenic in this group: 1.48 mg.

TERTIARY SYPHILIS: 8 cases; Wassermann positive.

No. of previous injections: 0-40.

Dose: 0.3 gm., 4 cases; 0.4 gm., 4 cases.

Smallest amount of arsenic: 0 after 0.3 gm. and 40 previous injections at irregular intervals; none for several months; female, white, aged 49.

Largest amount of arsenic: 1.83 mg. after 0.4 gm. and 5 previous weekly injections; male, white, aged 32.

Average amount of arsenic in this group: 0.32 mg.

LATENT SYPHILIS: 2 cases; Wassermann positive.

Smaller amount of arsenic: 0.343 mg. after 0.4 gm. and 21 injections; male, white, aged 42.

Larger amount of arsenic: 1.14 mg. after 0.3 gm., no previous injections; adult, female, white.

Average amount of arsenic in this group: 0.74 mg.

NONSYPHILITIC: 2 cases; Wassermann negative.

Smaller amount of arsenic: 0 after 0.4 gm. and no previous injections; male; white; aged 34.

Larger amount of arsenic: 0.0961 mg. after 0.4 gm. and no previous injections; male, white, aged 34.

Average amount of arsenic for this group: 0.05 mg.

CONGENITAL SYPHILIS: 1 case; Wassermann positive.

Amount of arsenic: 0.234 mg. after 0.3 gm. and 7 previous weekly injections; male, white, aged 17.

INTERVAL—5 DAYS

TERTIARY SYPHILIS: 4 cases; 2 with negative Wassermann; 2 with positive Wassermann.

No. of previous injections: 0-14.

Dose: 0.4 gm.

Smallest amount of arsenic: 0 after 0.4 gm. and 8 previous weekly injections; male, white, aged 26.

Largest amount of arsenic: 2.41 mg. after 0.4 gm., no previous injections; male, white, aged 39.

Average amount of arsenic in this group: 0.86 mg.

INTERVAL—1 WEEK

SECONDARY SYPHILIS: 8 cases; 1 with negative Wassermann; 7 with positive Wassermann.

No. of previous injections: 0-9.

Dose: 0.4 gm.

Smallest amount of arsenic: 0 after 0.4 gm. and 1 previous injection a week before; male, white, aged 29.

Largest amount of arsenic: 2.12 mg. after 0.4 gm. and 1 previous injection; male, white, aged 25.

Average amount of arsenic in this group: 0.85 mg.

TERTIARY SYPHILIS: 7 cases; Wassermann positive.

No. of previous injections: 0-49.

Dose: 0.3 gm., 1 case; 0.4 gm., 6 cases.

Smallest amount of arsenic: 0.133 mg. after 0.4 gm. and 2 previous weekly injections; male, white, aged 23.

Largest amount of arsenic: 4.14 mg. after 0.4 gm. and 1 previous injection a week before; male, white, aged 34.

Average amount of arsenic in this group: 1.0 mg.

LATENT SYPHILIS: 1 case; Wassermann positive.

Amount of arsenic: 0.931 mg. after 0.4 gm. and 4 previous weekly injections; male, white, aged 54.

CONGENITAL SYPHILIS: 2 cases; Wassermann positive.

Smaller amount of arsenic: 0.305 mg. after 0.3 gm. and 7 previous weekly injections; male, white, aged 15.

Larger amount of arsenic: 0.988 mg. after 0.4 gm. and 12 previous injections, this being the 4th of a second course; male, white, aged 20.

Average amount of arsenic in this group: 0.65 mg.

INTERVAL—10 DAYS

SECONDARY SYPHILIS: 2 cases; Wassermann positive.

Smaller amount of arsenic: 2.35 mg. after 0.4 gm. and 9 previous injections, the last 6 at weekly intervals, the first 3 every other day; male, white, aged 40.

Larger amount of arsenic: 2.82 mg. after 0.4 gm. and 3 previous injections at 4 and 6 day intervals; male, white, aged 23.

Average amount of arsenic: 2.59 mg.

INTERVAL—2 WEEKS

SECONDARY SYPHILIS: 3 cases; Wassermann positive.

No. of previous injections: 5-35.

Dose: 0.4 gm.

Smallest amount of arsenic: 0.343 mg. after 0.4 gm. and 35 previous injections, the last few at 2 and 3 week intervals; male, white, aged 29.

Largest amount of arsenic: 1.17 mg. after 0.4 gm. and 3 previous injections, at 2 day intervals; male, white, aged 30.

Average amount of arsenic in this group: 0.87 mg.

TERTIARY SYPHILIS: 5 cases; Wassermann positive.

No. of previous injections 0-44.

Dose: 0.4 gm.

Smallest amount of arsenic: 0.0428 mg. after 0.4 gm. and 16 previous injections, the last 2 weekly after 5 months' rest; male, black, aged 18.

Largest amount of arsenic; 1.73 mg. after 0.4 gm. and 44 injections the last 5 at weekly intervals after rest of 10 months; male, white, aged 45.

Average amount of arsenic in this group: 0.71 mg.

LATENT SYPHILIS: 1 case; Wassermann positive.

Amount of arsenic: 4.93 mg. after 0.4 gm. and 1 previous injection; male, white, adult.

INTERVAL—3 WEEKS

SECONDARY SYPHILIS: 1 case; Wassermann positive.

No arsenic present after 0.4 gm. and 26 previous injections, the last few irregularly; male, white, aged 29.

TERTIARY SYPHILIS: 4 cases; 3 with positive Wassermann, 1 negative.

No. of previous injections: 0-44.

Dose: 0.4 gm.

Smallest amount of arsenic: 0.751 mg. after 0.4 gm.; no previous injections; male, white, aged 34.

Largest amount of arsenic: 4.10 mg. after 0.4 gm. and 12 previous injections, the last 4 at weekly intervals; male, white, aged 45.

Average amount of arsenic: 1.78 mg.

INTERVAL—1 MONTH

SECONDARY SYPHILIS: 1 case; Wassermann positive.

Amount of arsenic: 1.66 mg. after 0.4 gm. and 7 previous injections 2 and 4 days apart; male, white, aged 39.

TERTIARY SYPHILIS: 3 cases; Wassermann positive.

No. of previous injections: 3-67.

Dose: 0.4 gm.

Smallest amount of arsenic; 0 after 0.4 gm. and 67 previous injections; male, white, aged 42. (The patient is an old neurosyphilitic receiving treatment once or twice a month.)

Largest amount of arsenic: 1.99 mg. after 0.4 gm. and 13 previous injections, the last few weekly; male, white, aged 25.

Average: 1.102 mg.

INTERVAL—5 WEEKS

TERTIARY SYPHILIS: 1 case; Wassermann positive.

No arsenic present after 0.4 gm. and 44 previous injections, the last a year before; male, white, aged 45.

INTERVAL—2 MONTHS

SECONDARY SYPHILIS: 2 cases; Wassermann positive.

Smaller amount of arsenic: 0.218 mg. after 0.4 gm. and 5 previous injections; male, black, aged 23.

Larger amount of arsenic: 0.810 mg. after 0.4 gm. and 13 previous injections, the second course being irregularly taken every 2 or 3 months; male, white, aged 25.

Average amount of arsenic: 0.51 mg.

INTERVAL—3 MONTHS

TERTIARY SYPHILIS: 2 cases; Wassermann positive.

Smaller amount of arsenic: 0.8009 mg. after 0.4 gm. and 17 previous injections at irregular intervals after the first course; male, white, aged 29.

Larger amount of arsenic: 0.88 mg. after 0.4 gm. and 30 previous injections; male, black, aged 28.

Average amount of arsenic: 0.84 mg.

INTERVAL—6 MONTHS

SECONDARY SYPHILIS: 1 case; Wassermann positive.

Amount of arsenic: 0 after 0.4 gm. and 7 previous injections; male, white, aged 27.

INTERVAL—7½ MONTHS

TERTIARY SYPHILIS: 1 case; Wassermann positive.

Amount of arsenic: 0.561 mg. after 0.4 gm. and 13 previous injections, the last 6 at weekly intervals; male, white, aged 53.

TABLE V

Table V shows the rate of retention of arsenic on individuals from whom more than one specimen was obtained.

TIME INTERVAL	SERIAL #1057	SERIAL #1171	SERIAL #783	SERIAL #545	SERIAL #569	SERIAL #879	SERIAL #885	SERIAL #85	SERIAL #17	SERIAL #11	SERIAL #14	SERIAL #89	SERIAL #51	SERIAL #67	SERIAL #99	SERIAL #52	SERIAL #45
Immediate	1.25	0.555	2.9														
10 min.				0.434	0.974	2.22	4.10										
20 "								1.13	1.64	1.03	0.734	0.803	Trace	2.72	0.980	1.820	0.479
30 "				1.30	0.327		1.36										
40 "								0.310	1.01	0.202	0.295	1.95	2.41	1.63		1.95	1.002
50 "						3.21											
60 "									1.65	0.14	1.24	0.374	0.123	0.584	2.76	0.368	1.92
24 hours																	
48 "	0.253																
72 "																	
1 week		0.124															
2 "																	
3 "																	
6 "			0.32														
10 months																	
Dose	0.4	0.4	0.3	0.3	0.3	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.3

TIME INTERVAL	SERIAL #61	SERIAL #58	SERIAL #1126	SERIAL #514	SERIAL #565	SERIAL #568	SERIAL #591	SERIAL #539	SERIAL #547	SERIAL #541	SERIAL #1236	SERIAL #2241	SERIAL #2374	SERIAL #2414	SERIAL #2376	SERIAL #2327	SERIAL #2656
Immediate																	
10 min.																	
20 "	1.13	1.7															
30 "																	
40 "	1.52	0.311															
50 "																	
60 "	0.336	0.2208															
24 hours			0.14	0.029	0.062	1.37	0.326	0.0315	7.2	0.232	Trace	1.32	0.167	0	0.488		
48 "			0.108	Trace	0.050	0.72	0.708	Trace	0.034	0.113	0.030	0.463	0.101	1.39	0.857	0.932	
72 "			0.289								0.052	1.21				1.13	
1 week																	
2 "																	0.343
3 "																	0.
6 "																	
10 months		None															
Dose	0.4	0.4	0.5	0.4	0.3	0.3	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.3	0.4	0.4

In summarizing these tables it is observed that for the intervals varying from blood taken immediately after injection to a period of 2 weeks, the following average values for the arsenic per 100 gm. of dried specimen were found:

TABLE VI

INTERVAL	CHART I	CHART III
0+	4.28	4.21
5 min.	....	1.40
10 min.	0.88	1.00
15 min.	0.98	1.15
20 min.	1.29	0.80
30 min.	1.00	0.68
40 min.	0.94	....
50 min.	1.86	....
60 min.	1.07	0.54
120 min.	....	0.47
24 hrs.	0.25	0.34
48 hrs.	0.22	0.56
72 hrs.	....	0.47
96 hrs.	....	0.47
120 hrs.	....	0.86
7 days	1.01	1.00
2 weeks	....	1.00

Table VI shows the average retention by individuals based upon the values obtained from Tables I and III. Table VI is a continuation of Table V with the results obtained as a result of averages in Tables I and III.

Only the values for Column 3 were charted inasmuch as there was a rather close agreement between those found in the 2 series of observations. These observations were made over a period of 1 year with the idea of checking up on patients in various stages of the disease, and in most instances it will be noted that a close agreement in values exists. The widest discrepancies were met with at the fifty minute, sixty minute, and forty-eight hour intervals.

As previously stated, the values in Column 3 were recorded as the more exact inasmuch as the timing of the blood specimens was made with an accuracy of about thirty seconds, whereas a little greater variation occurred in those found in Column 2.

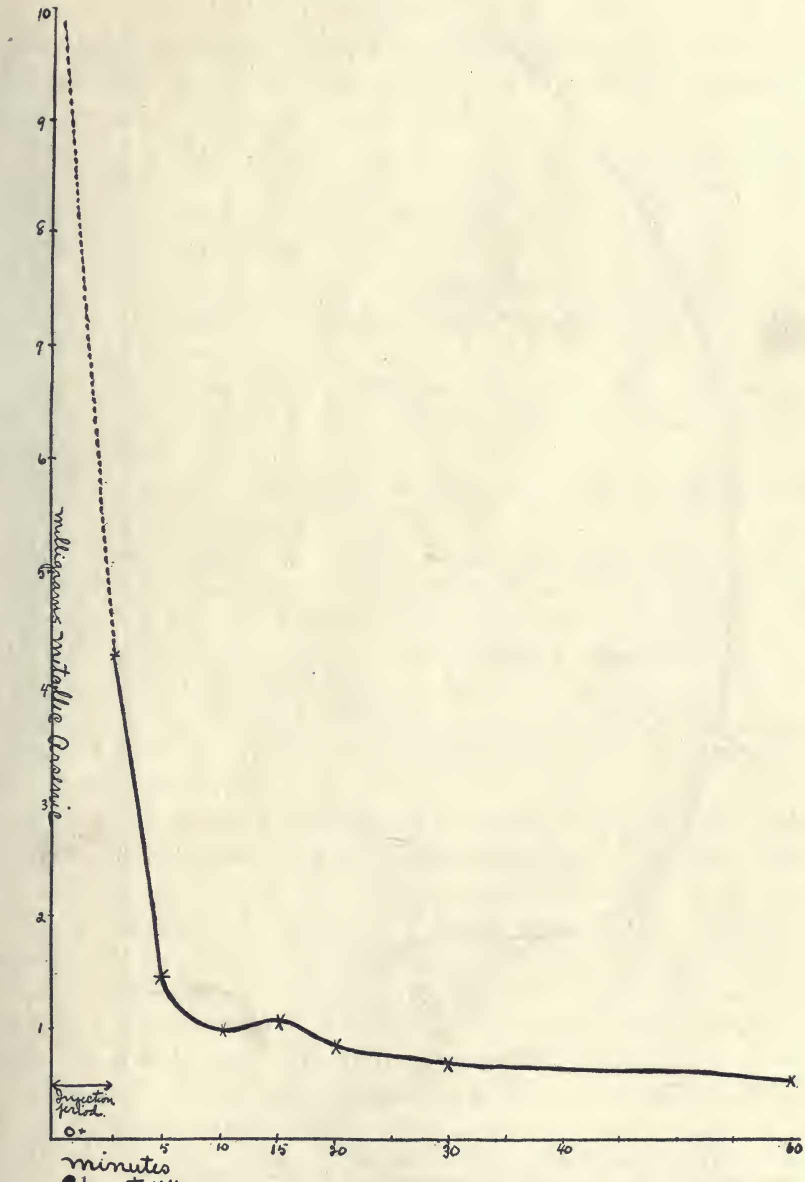

Chart VII

Chart VII graphically shows the arsenic present in the blood stream at varying intervals as illustrated in Column III of Table VI. Milligrams of metallic arsenic in 100 grams of dried specimen are plotted against intervals in minutes. The dotted line shows the theoretical fall in arsenic content of the blood during the injection interval.

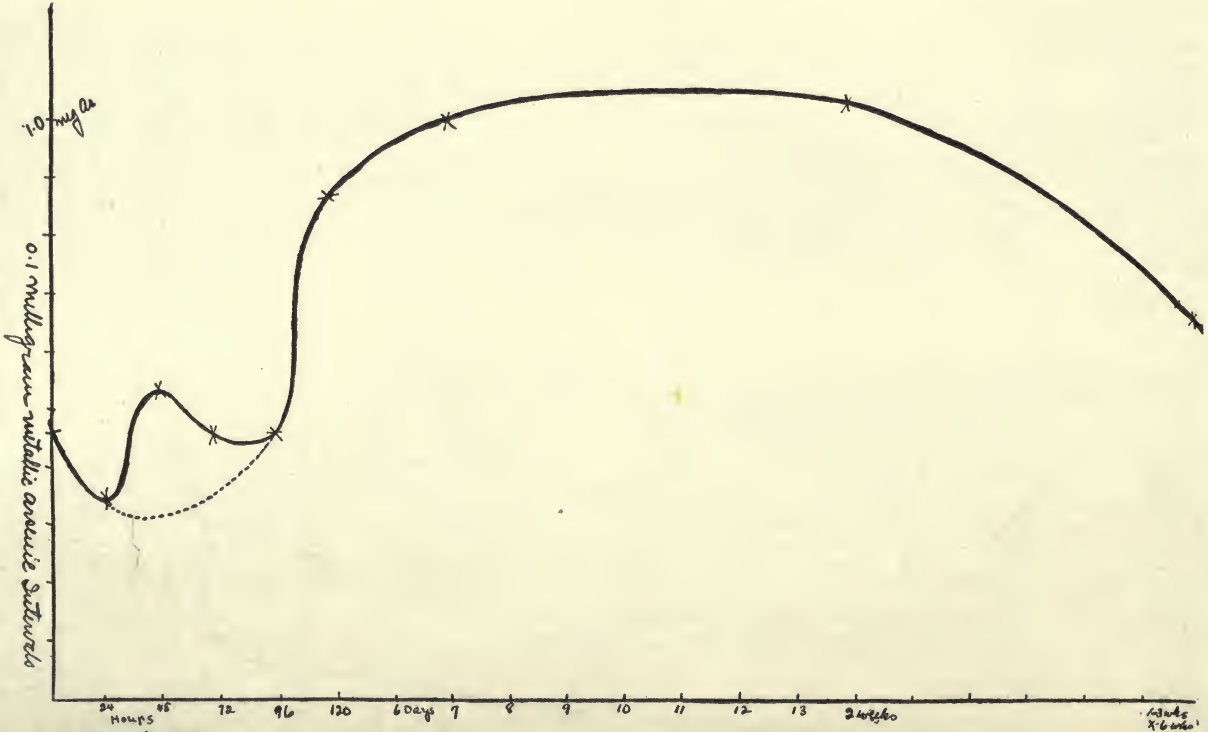

Chart VIII

Chart VIII is a continuation of Chart VII, showing a blood retention value of metallic arsenic at intervals up to 6 weeks. It should be noted that the scale is *magnified*. The dotted line shows the probable value of arsenic at this interval and the heavy line indicates a slight error in the method. *Tenths* of milligrams of metallic arsenic are plotted against time intervals in hours and weeks.

SUMMARY

I. Analysis of blood taken *immediately* after the completion of the injection showed that 60 per cent of the arsenic injected has been localized outside of the blood stream.

II. The maximum quantity of arsenic in the blood stream based upon average values is found immediately after injection. This value expressed in milligrams of metallic arsenic per 100 grams of dried specimen is 4.21.

III. Observations at later intervals up to one day indicated that the arsenic equilibrium in the blood gradually becomes lower, based on average values.

IV. There was a marked increase in arsenic after a period of one day with a gradual diminution at later intervals, based on average values.

V. These results were based on the average of all types of patients in all stages of the disease.

VI. Certain individuals having an arsenic idiosyncrasy or predisposition to arsenical intoxication show abnormal values both high and low for any given interval (partition coefficient).

VII. Complete classification of all patients in regard to age, sex, previous treatment, and stage of the disease is found in the accompanying tables (II and IV) in correlation with the specimen used, and the arsenic content expressed in milligrams per 100 grams of the dried specimen.

VIII. Through these analyses it is hoped that a suitable interval for securing blood in the Swift-Ellis method of procedure can be selected and tending to standardize the procedure.

IX. It is apparent that certain cases have a high "partition coefficient" making difficult the selection of the most suitable interval for obtaining the salvarsanized serum. This point is illustrated by observing the "high" and "low" partition values tabulated in Tables I and III under "immediate" intervals.

X. Rapid localization of the drug may be a warning for certain latent arsenical intoxications.

XI. It is observed that there are two well-defined groups of individuals responsible for irregularity of arsenical fluctuations in excretion and retention after intravenous injection of salvarsan. These may be classified as "short period" and "long period."

XII. Variations of arsenic content and ''possible'' variation of therapeutic activity were eliminated by using the same control number of the drug throughout the entire investigation.

XIII. By examination of Tables I and III it is observed that the rate of partition between blood and tissues varies with individual patients and on this basis the efforts in bringing about arsenic saturation in an individual demand careful observation of the patient.

XIV. Analyses of Tables I and III are found in Tables II and IV.

XV. Table V indicates the ''partition coefficient'' in patients from whom more than one specimen of blood was obtained, the interval being indicated in the Table.

XVI. Clinical discussion will be found in the succeeding articles dealing with the determination of arsenic after the intravenous administration of neosalvarsan and silver salvarsan.

XVII. Discussion of other findings tabulated in this paper will be found in a later publication.

A CLINICAL AND BIOCHEMICAL STUDY OF NEUROSYPHILIS

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PART I

THE ARSENIC CONTENT OF THE SPINAL FLUID AFTER THE INTRAVENOUS ADMINISTRATION OF SILVER ARSPHENAMINE

THE primary purpose of this study was to obtain information concerning the permeability of the neurovascular apparatus to the complex protein-arsenic molecule or its active therapeutic cleavage product after the intravenous administration of silver arsphenamine. Through the kindness of Professor Gies, of the Department of Biologic Chemistry, College of Physicians and Surgeons, ample space and chemical facilities were placed at our disposal and the Neurological Department of the Vanderbilt Clinic afforded the clinical material.

This problem was approached at first only in a general manner. The early results suggested many points hitherto unthought of and it became apparent that it would be necessary to formulate a definite scheme for attacking the whole problem in a sequential manner. In order to accomplish this on a scale adequate for our needs we were confronted with the necessity of enlarging our staff of assistants and organizing it into an efficient team. Acknowledgment and appreciation is expressed to Mr. H. A. Metz for placing at our disposal a part of the necessary funds for the chemical portion of this investigation and to the Commonwealth Fund through the Research Department of the New York Neurological Institute for support of the clinical portion of the investigation.

The original staff of two or three workers was enlarged to include a clinical supervisor, with one technical assistant; a chemical supervisor, with one trained chemist as first assistant, two technical assistants, and three clerical assistants. We take this occasion to express grateful appreciation for the industrious and sympathetic cooperation of our staff: Mrs. J. Macklem, Misses N. L. Bacon, Adelaide Van Holten, Marion Groehl, and Marjorie Lockhart.

The analytical methods used in this investigation are identical with those that were described in detail by Fordyce, Rosen and Myers. (Amer. Jour. Med. Sc., Vol. 164, pp. 493 to 514, October, 1922.) This investigation was planned along many of the same lines previously outlined by the above authors (p. 494 ibid.) and therefore some of our problems closely parallel each other, except that this investigation is limited to silver arsphenamine and the discussion definitely follows neurological hypotheses. In the main, each series of articles expands some of the ideas pointed out in Public Health Reports, Reprint 520, p. 881, 1919.

The work has attained proportions scarcely dreamed of at its beginning. Two years have already elapsed and only a few phases of the problem have been covered. The results will be published serially with the hope that they may stimulate contributions from other workers that will assist in solving some of the problems concerning the physiologic chemistry and relative therapeutic efficiency of the arsenicals.

Some of the questions to which we would seek answers are:

1. How much arsenic appears in the spinal fluid after intravenous administration of silver arsphenamine?

2. How rapidly does arsenic enter the spinal fluid and how rapidly is it eliminated?

3. Does spinal drainage influence the arsenic content of the spinal fluid?

4. Does the amount of arsenic vary with the type of pathologic lesion?

5. Do age and occupation influence the arsenic content of the spinal fluid?

6. Does the method of administration of the drug have any influence on the arsenic content of the spinal fluid?

7. Is there any relation between the amount of arsenic in the spinal fluid and in the neural tissues?

8. At what intervals after intravenous administration do the spinal fluid and neural tissues contain the greatest amount of arsenic?

9. What effect, if any, upon permeability has the repeated intraspinal administration of silver arsphenamine?

10. Does arsenic ever accumulate in the spinal fluid to the point of danger?

11. How much arsenic is administered intraspinously by the Swift-Ellis method?

12. What is the optimum period after the intravenous administration of silver arsphenamine to withdraw blood?

13. How does the amount of arsenic in whole blood serum and clot compare?

14. How soon after the blood is drawn should the serum be separated?

15. Can the permeability of neural blood vessels to arsenic be influenced by physical or therapeutic factors?

16. Is there any relation between the arsenic content of the spinal fluid or neural tissues and the symptomatic progress?

17. Is there any relation between the arsenic content of the spinal fluid or neural tissues and the pathology (cytologic, serologic or chemical)?

18. What is the relation between total solids and the arsenic content of the spinal fluid? Between the total solids and other fluid pathology?

19. What is the relation between the total solids and the neural tissue pathology?

20. What is the relation between the total solids in the spinal fluid and the symptomatic progress?

21. How does therapy influence the total solids in the spinal fluid?

The results, embodied in this report, are limited almost exclusively to a group of cases that were receiving silver arsphenamine intravenously. Specimens of spinal fluid were obtained from two to ninety-six hours after the intravenous administration of the drug.

With a few exceptions none of the cases received, during the period of study, any intraspinous injections of auto-arsphenaminized or fortified serum. The amount of fluid withdrawn varied from twelve to thirty cubic centimeters, therefore the technic was essentially that of spinal drainage.

The weight of the moist specimen was first obtained and after evaporation the dry residue was weighed. The percentage of solids was calculated from these results.

For uniformity it was decided to express all results on the dry basis, i.e., mgm. of arsenic per 100 gm. of dry residue. A trace of arsenic signifies an amount too minute for quantitative estimation (less than 1 part per 2,000,000 or .05 mgm. per cent).

The dosage of silver arsphenamine was from 0.1 to 0.2 gm. Our experience with this preparation in neurosyphilitics consists of 2490 injections during a period of 24 months. This class of patients tolerate this arsenical well. Unpleasant reactions occurred only occasionally and jaundice was infrequent. As a class, neurosyphilitics are not vigorous or robust in health. Physically they are far below par, but the majority of cases tolerate well doses of 0.2 gm.

Many of our cases, in fact most of them, are far advanced when we first see them. They represent a type of human derelict that does not afford opportunity for spectacular clinical or therapeutic results. The clinical signs of neurologic dysfunction are frequently due to neural degeneration or scar formation. The ectodermal components of the central nervous system have no power of regeneration. Neural scars whether mesodermal or ectodermal cannot be removed. Our therapeutic aim, therefore, is to destroy, if possible, the injurious agent—the Treponema pallidum—and to prevent the further progress of the disease. In exudative forms of mesodermal neurosyphilis complete restoration of function can be attained but much more frequently the best that we can hope for is the preservation of the already existent function from further impairment.

For reasons above suggested our therapy has to be individualized. We sometimes give mercury and the arsenicals at the same time but more frequently alternate them and vary the particular preparation in accordance with the toleration and the therapeutic result obtained. Potassium iodide is, in some cases, combined with mercury either as a separate preparation or in the form of mixed treatment. We administer arsphenamine in courses of 6 to 8 weekly doses and mercury in courses of 12 to 15 weekly intramuscular injections when well tolerated and not contraindicated.

Our intraspinous therapy consists of the drainage method, Swift-

Ellis method, and the latter plus in vitro arsphenamine fortification. Intraspinous treatments are administered at intervals of from two weeks to two months. In vitro fortification of serum is employed only in deep seated lesions that fail to respond to the other methods of treatment. With a few exceptions it is always combined with intravenous arsenical therapy.

To facilitate the analysis and interpretation of our results they have been tabulated in accordance with the interval between the intravenous administration and the spinal drainage. The classification previously published by one of us which is schematically indicated below was adhered to.

Peripheral Neurosyphilis
- Somatic,—Cranial and peripheral nerves, their ganglia and end organs.
- Sympathetic,—Sympathetic nerves, their chain ganglia and terminal arborizations.

Central Neurosyphilis

Topographical
- Cerebral
- Spinal
- Cerebrospinal

Germ layer — *Structural*
- Mesodermal—Meningeal
  Vascular
  Menigo-vascular
- Ectodermal—Parenchymatous
- Mixed Forms—Involving both mesodermal and ectodermal elements.

Until contradictory facts are presented we subscribe to the prevailing opinion that syphilitic foci are implanted in the neural structures during the period of generalization when the skin and its appendages, the mucous membranes and glands are involved. The truth of the maxim, "seeing is believing," bodes ill for the potential neurosyphilitic. The objective manifestations in the skin, mucous membranes and glands make their impression on patient and physicians and encourage therapy. Their disappearance is too frequently the indicator for cessation of therapy.

Nature's protective agencies in the nervous system mask objectively the first stages of the spirochetal action there. The absence of symptomatic manifestation of impaired nerve function during the early period of spirochetosis is due, in our opinion, to the superficial location of the spirochetes and Nature's temporary defense against them. By the term superficial we mean in relation to the neural structures that initiate, transmit or function as terminal stations for nerve impulses. Such superficial sites are the meninges, the capillaries, the lymph spaces and the glial zones (membranae limitans gliae superficialis and perivascularis) immediately contiguous thereto. Superficial, in this sense, means to us epineuronal rather than endoneuronal, in the supportive or reticular structures rather than in the parenchymatous or nuclear ones. Pathologically the process is primarily exudative rather than degenerative. To be sure, the integrity of the neurones may be compromised by small wedge shaped areas of exudation, which extend from the meninges or blood vessels and encroach mechanically upon neuronal pathways.

Similarly clinical states indicative of destructive nuclear lesions may be dependent upon a primary vascular pathology. Ischemic necrosis in cases of obliterative endarteritis furnishes an example of this. In other cases, mesodermal and ectodermal elements may be simultaneously affected.

But the pathology briefly sketched above must be clearly contrasted with the type that is from the beginning, in so far as clinical symptoms and correlated pathologic observations indicate, deeply situated, nuclear in location, and degenerative in form.

We believe that the localization of syphilitic lesions to the mesodermal structures—meninges and blood vessels—is due to natural factors of resistance and immunity and perhaps to variations in the virulence of spirochetal strains. The limitation of the progress of syphilitic neuropathology can, in our opinion, be influenced by reenforcing the efforts of Nature with properly directed therapy. The spirochete may overwhelm before Nature can organize and launch a successful defense. We have observed clinically and pathologically acute fulminating cases of generalized syphilis followed by early death.

The subject matter of this report is based upon an examination of 239 fluids from 151 patients. It compromises a well diversified group of clinical and pathologic varieties of neurosyphilis.

The topographical location of the pathologic anatomy was represented as follows:

Cerebral	59
Spinal	96
Cerebrospinal	79
Peripheral	1
Unclassified	4
	239

The location of the pathologic anatomy in relation to the germ layer derivation was represented as follows:

Mesodermal	104
Ectodermal	108
Mixed	22
Peripheral	1
Unclassified	4
	239

GENERAL SURVEY

If one considers the totality of results (Table I) in relation to the interval between the arsenical administration and the lumbar puncture, it is apparent that a considerable quantity of arsenic enters the spinal fluid within the first two hours after intravenous administration (11.548 mgm. per cent). Its passage from the blood

TABLE I

INTERVAL	NO. OF FLUIDS	NO. OF CASES	AS. CONTENT IN MGM. % MAXIMUM	AVERAGE
2 hours	115	62	143.	11.548
24 hours	45	34	155.	7.185
48 hours	46	30	74.6	7.912
72 hours	33	25	192.0	12.589
	239	151		

TABLE II

INTERVAL	ARSENIC PRESENT SUFFICIENT FOR QUANTITATIVE ESTIMATION	ARSENIC ABSENT OR PRESENT IN TRACE
2 Hours	78%	22%
24 Hours	70%	30%
48 Hours	60%	40%
72 Hours	68%	32%

stream to the fluid is then either temporarily arrested or the elimination from the fluid is more rapid than the passage into it.

One may infer that soon after intravenous administration of silver arsphenamine some or all of the drug enters into physical and chemical combination with the tissues. Later there occurs a stage of colloidal equilibrium, and the diameter of the colloidal particles becomes such that, through phenomena of osmosis and diffusion or by other means, the arsenic passes through the tissue membranes. That some such mechanism operates is indicated by the amount of arsenic in the spinal fluid at the end of the seventy-two hours (12.589 mgm. per cent) which exceeds the amount present at twenty-four and forty-eight hours by nearly 5 mgm. per cent. This feature will be discussed in a later paper.

One is forced to conclude that the arsenic is in a state unsuitable for passage through the chorioid plexus and the question suggests itself whether the arsenic is in the circulating blood or in the viscera. If in the circulating blood is it in the serum or combined with the cells? If in the viscera is it in the neural tissues?

TWO HOUR GROUP

The two hour group consisted of 115 specimens from 62 cases. Arsenic was present in amounts sufficient for quantitative determination in 78 per cent of the cases. The largest quantity of arsenic, 143 mgm. per 100 gm. was from a case (No. 29 D.C.) of spinal meningovascular syphilis in a male aged forty diagnosed clinically as hypertrophic cervical meningitis. This case had been under our care for five months preceding the examination, during which period two injections of arsphenamine and six of silver arsphenamine had been administered intravenously and a series of fifteen intramuscular mercurial injections had been given. The blood Wassermann was positive. In the spinal fluid there were nine cells, the globulin was two-plus, the Wassermann and Vernes reactions were positive and the colloidal gold curve was of the paretic type. Under combined intravenous and intraspinal therapy consisting of 2 arsphenamine, 33 silver arsphenamine, 30 mercurial, 8 intraspinal treatments, and two spinal drainages over a period of 18 months, the spinal fluid findings became negative. There was functional improvement and an apparent arrest of the progress of the pathology.

The blood Wassermann and Vernes reactions remained positive. Treatment is still being pursued.

In thirteen specimens from nine cases (14½ per cent) no arsenic was recovered from the spinal fluid and in seven specimens from five cases (8 per cent) it was apparent only in a trace. The classification and pertinent details of these fourteen cases follow:

DIAGNOSTIC CLASSIFICATION	ARSENIC ABSENT		ARSENIC PRESENT IN TRACE	
	FLUIDS	CASES	FLUIDS	CASES
Mesodermal—Cerebral	0	0	1	1
Mesodermal—Cerebrospinal	0	0	2	2
Ectodermal—Cerebral (Paresis)	3	2	0	0
Ectodermal—Spinal (Tabes)	6	5	3	2
Mixed —Cerebrospinal	4	2	1	1
Total	13	9	7	5
Case per cent	14.5		8	

One specimen from a case of unconfirmed syphilis with an incomplete tabetic syndrome which contained only a trace of arsenic is not included.

ARSENIC ABSENT

CASE 1.—Nos. 50, 51, W. E. Cerebrospinal, mixed form, almost complete bilateral optic atrophy, male, age fifty-seven, painter.

First Examination: Blood—Wassermann four plus. Spinal fluid—cells 20, globulin four plus, Wassermann four plus with 0.4 c.c., colloidal gold 2233210000.

Treatment—29 months: Arsphenamine, 23; Silver arsphenamine, 5; Mercurial, 36; Intraspinal, 2; Spinal drainage, 4.

Last Examination: Blood—Wassermann four plus. Spinal fluid—cells, 4, globulin trace, Wassermann negative with 2.0 c.c. alcohol antigen ice-box fixation, one plus with 2.0 c.c. cholesterin antigen warm fixation, colloidal gold 223332100.

Clinically there was but slight if any improvement in vision but the acuity had not diminished.

CASE 2.—Nos. 55, 56. M. W. Cerebrospinal, mixed, moderate bilateral optic atrophy, male, age, forty-eight.

First Examination: Blood—Wassermann four plus, Spinal fluid—cells 28, globulin one plus, Wassermann four plus in 0.5 c.c., Vernes positive, colloidal gold 5554421000.

Treatment—14 months: Silver arsphenamine, 23; Mercurial, 31; Intraspinal, 4; Spinal drainages, 9.

Last Examination: Blood—Wassermann three plus. Spinal fluid—negative.

There was general clinical improvement with subjective improvement of visual acuity.

CASE 3.—No. 61, M. J. Paretic syndrome, depressed type, male, age thirty-two, clerk. Deterioration moderate. Insight well preserved.

First Examination: Blood—Wassermann four plus. Vernes positive. Spinal fluid—typically positive in all phases.

Treatment—6 months: Arsphenamine, 8; Silver arsphenamine, 6; Mercurial, 15; Intraspinal, 3; Spinal drainage, 1.

There was no noticeable objective improvement. The treatment was discontinued voluntarily by the patient. Death ensued within 30 months.

CASE 4.—Nos. 62, 63, F. B. Paretic syndrome, euphoric type, male, age forty-seven, actor. The blood and fluid findings were similar to Case 3. Mental deterioration was advanced, very little insight being preserved. Death ensued in five months.

CASE 5.—Nos. 77, 78, J. G. Tabetic syndrome, male, age forty-one, mechanic.

First Examination: Blood—Wassermann four plus. Spinal fluid—cells 46, globulin 2 plus. Wassermann four plus in 0.5 c.c., Vernes positive. Collodial gold 5555554310.

Treatment—29 months: Arsphenamine, 5; Silver arsphenamine, 22; Mercurial, 59; Intraspinal, 17; Spinal drainage, 11.

Last Examination: Blood—Wassermann three plus.

Spinal fluid—no change except a drop in the cell count to 7.

Clinically the subjective symptoms of pain have been relieved. The ataxia is not progressing. The patient can earn sufficient remuneration to support himself.

CASE 6.—No. 83, M. L. Tabetic syndrome, male, age forty-six, tailor.

First Examination: Blood—Wassermann three plus. Spinal fluid—3 cells, globulin one plus, Wassermann three plus in 2.0 c.c., Vernes positive, colloidal gold 0000000000.

Treatment—4 months: Silver arsphenamine, 9; Spinal drainages, 2.

CASE 7.—No. 87, H. M. Tabetic syndrome, male, age fifty-six, bookkeeper.

Last Examination: Blood—Wassermann negative. Spinal fluid—negative.

First Examination: Blood Wassermann three plus. Spinal fluid—cells 48, globulin 2 plus, Wassermann positive, Vernes positive, colloidal gold 5555443210.

Treatment—18 weeks: Silver arsphenamine, 18; Spinal drainage, 3.

Last Examination: Blood—Wassermann negative. Spinal fluid—cells 7, globulin 1 plus, Wassermann positive in 1 c.c., Vernes positive, colloidal gold 4441100000.

CASE 8.—No. 98, J. R. Tabetic syndrome, male, age forty-eight, butcher.

First Examination: Blood—Wassermann three plus. Spinal fluid—cells 3, globulin normal, Wassermann four plus in 2.0 c.c., Vernes positive, Colloid gold 5532111000.

Treatment—20 months: Arsphenamine, 10; Silver arsphenamine, 20; Spinal drainages, 6.

Last Examination: Blood—Wassermann negative. Spinal fluid—negative in all phases except collodial gold which remained unchanged.

Objectively and subjectively the clinical symptoms indicated arrest.

CASE 9.—No. 100, J. T. Tabetic syndrome, male, age fifty.

First Examination: Blood—Wassermann four plus. Spinal fluid—cells 62, globulin 4 plus, Wassermann positive in 0.2 c.c., Vernes positive, colloidal gold 5555431000.

Treatment—24 months: Arsphenamine, 9; Silver arsphenamine, 8; Mercurial, 10; Intraspinal, 12; Spinal drainage, 1.

Last Examination: Blood—Wassermann negative. Spinal fluid—negative in all phases. Clinically there was arrest.

ARSENIC PRESENT IN A TRACE

CASE 10.—No. 21, A. B. Cerebral meningovascular syphilis with beginning optic atrophy, male, age thirty-seven, salesman.

First Examination: Blood—Wassermann four plus; Vernes positive. Spinal fluid—cells 3, globulin normal, Wassermann 4 plus in 1.0 c.c., Vernes positive, colloidal gold 1112533211.

Treatment—30 months: Arsphenamine, 7; Silver arsphenamine, 29; Mercurial, 30; Intraspinal, 1; Spinal drainage, 3.

Last Examination: Blood—Wassermann one plus. Spinal fluid—negative except the colloidal gold 5555543210. Clinically there was complete arrest.

CASE 11.—Nos. 47, 48, P.P. Cerebrospinal meningovascular, male, age forty-two, packer.

First Examination: Blood—Wassermann four plus; Vernes positive. Spinal fluid—cells 9, globulin trace, Wassermann four plus in 0.5 c.c., Vernes positive, colloidal gold 5444210000.

Treatment—18 months: Arsphenamine, 14; Silver arsphenamine, 20; Mercurial, 30; Intraspinal, 4; Spinal drainages, 11.

Last Examination: Blood—Wassermann doubtful. Spinal fluid—negative except the colloidal gold 2223332100.

There was decided clinical improvement and apparent arrest.

CASE 12.—No. 54, M. W. Same as Case 2.

CASE 13.—No. 67, 68, C. C. Tabetic syndrome, female, age thirty-four, housewife.

First Examination: Blood—Wassermann 3 plus. Spinal fluid—cells 39, globulin 1 plus, Wassermann 4 plus in 2.0 c.c., Vernes negative, colloidal gold 2553322100.

Treatment—29 months: Arsphenamine, 3; Silver arsphenamine, 15; Mercurial, 44; Intraspinal, 1; Spinal drainages, 4.

Last Examination: Blood—Wassermann negative. Spinal fluid—negative, colloidal gold 0023222211.

CASE 14.—No. 75, J. G. Same as Case 5.

It is significant that this group of fourteen cases with only a trace or no arsenic in the spinal fluid represent pathologically deep seated lesions. They represent approximately 22 per cent of the whole group. The two paretics have died. Of the remainder six were tabetic and three had optic atrophy.

TWENTY-FOUR HOUR GROUP

This group consisted of 45 specimens from 34 cases. Arsenic was present in an amount sufficient for quantitative determination in 70 per cent of the cases. The highest amount of arsenic recovered was 155 mgm. per 100 gm. This result was from a case of cerebrospinal syphilis of mixed form with extreme bilateral optic atrophy, male, age forty-five (No. 24 T.S.), peddler. He had been under treatment constantly for three and a half years before the fluid was examined for arsenic and had received treatment as follows:

Sixty arsphenamine, 1 silver arsphenamine, 79 mercurial and 21 intraspinal injections. On admission the blood Wassermann was four plus and the spinal fluid was four plus in 1.0 c.c., with no cells or globulin, colloidal gold 1122210000. After the treatment outlined above the spinal fluid was rendered negative but the blood remained four plus. There has been apparently complete arrest of all clinical symptoms.

Four cases or 12 per cent showed no arsenic and six cases or 18 per cent only a trace. The classification and details of the cases follow:

DIAGNOSTIC CLASSIFICATION	ARSENIC ABSENT		ARSENIC PRESENT IN TRACE	
	FLUIDS	CASES	FLUIDS	CASES
Mesodermal (Cerebrospinal)	2	2	3	3
Ectodermal (Paretic syndrome)	1	1	0	0
Ectodermal (Tabetic syndrome)	1	1	2	2
Mixed (Cerebrospinal)	0	0	1	1
Total	4	4	6	6
Case per cent	12		18	

ARSENIC ABSENT

CASE 1.—No. 2, H. A. Cerebrospinal meningovascular, male, age forty, salesman.

First Examination: Blood—Wassermann negative. Spinal fluid—cells 3, globbulin 1 plus, Wassermann 2 plus with 2.0 c.c., Vernes negative, colloidal gold 2221100000.

Treatment—12 months: Silver arsphenamine, 14; Mercurial, 18; Intraspinal, 7.

Last Examination: Spinal fluid—unchanged except that the Wassermann reaction was 4 plus with 1.0 c.c.

Clinically there was no improvement and mental changes suggestive of cerebral endarteritis appeared. Death from cerebral hemorrhage occurred sixteen months after admission.

CASE 2.—No. 10, M. G. Cerebrospinal meningovascular, male, age thirty.

First Examination: Blood—Wassermann 2 plus. Spinal fluid—cells 9, globulin normal, Wassermann 2 plus with 2.0 c.c., colloidal gold 2211110000.

Treatment: Treatment was only continued for a short time and the patient has been lost track of.

CASE 3.—No. 27, A. S. Paretic syndrome (?), male, age thirty-nine, laborer.

First Examination: Blood—Wassermann doubtful. Spinal fluid—cells 3, trace of globulin, Wassermann 4 plus with 10 c.c., colloidal gold 5554333210.

Treatment—10 months: Silver arsphenamine, 14; Mercurial, 9; Intraspinal, 8.

Last Examination: Blood—Wassermann negative. Spinal fluid showed no essential change except a slight diminution of the colloidal gold curve 4333321100.

CASE 4.—No. 30, C. C. Tabetic syndrome, male, age fifty, musician.

First Examination: Blood—Wassermann 4 plus. Spinal fluid—cells 4, globulin 1 plus, Wassermann 2 plus with 2.0 c.c., Vernes positive, colloidal gold 1112211100.

Treatment—12 months: Arsphenamine, 6; Silver Arsphenamine, 3; Mercurial, 24; Intraspinal, 2.

Last Examination: Blood—Wassermann 1 plus, Vernes negative. Spinal fluid—cells 10, a trace of globulin, Wassermann negative in 2.0 c.c., Vernes positive, colloidal gold 1111110000.

Clinically there was apparent arrest.

ARSENIC PRESENT IN TRACE

CASE 5.—No. 9, C. B. Cerebrospinal meningovascular, male, age forty-two, City Fireman.

First Examination: Blood—Wassermann 4 plus, Vernes positive. Spinal fluid—cells 19, globulin 2 plus, Wassermann 4 plus with 0.5 c.c., Vernes positive, colloidal gold 5554332100.

Treatment—28 months: Arsphenamine, 10; Silver arsphenamine, 32; Mercurial, 45; Intraspinal, 22.

Last Examination: Blood—Wassermann unchanged. Spinal fluid—showed a reduction in the cell count and colloidal curve to normal but the Wassermann remained unchanged.

Clinically there was subjective and objective improvement and the hazardous duties of his occupation were resumed. A sudden termination from a cerebral vascular accident may be looked for.

CASE 6.—No. 19, H. R. Cerebrospinal meningovascular, male, age forty-three, farmer.

First Examination: Blood—Wassermann negative. Spinal fluid—cells 24, globulin 1 plus, Wassermann 2 plus with 2.0 c.c., colloidal gold 0001110000.

Treatment—3 months: Silver arsphenamine, 11; Mercurial, 11; Intraspinal, 6.

Last Examination: Blood—Wassermann negative, Vernes reaction negative. Spinal fluid—completely negative.

All symptoms were relieved.

CASE 7.—No. 21, J. S. Cerebral meningovascular, male, age fifty-three, clerk.

First Examination: Blood—Wassermann 2 plus. Spinal fluid—cells 80, globulin 2 plus, Wassermann 4 plus with 0.5 c.c., colloidal gold 5555322000, Vernes positive.

Treatment—15 months: Silver Arsphenamine, 23; Mercurial, 32; Intraspinal, 14.

Last Examination: Blood—Wassermann unchanged. Spinal fluid—cell 1, trace of globulin, Wassermann 4 plus, with 1.0 c.c., colloidal gold 1111100000.

There has been an amelioration of the subjective symptoms but no change objectively.

CASE 8.—No. 23, M. W. Same as Case 2 in 24 hour group.

CASE 9.—No. 28, P. B. Tabetic syndrome, female, age thirty-five, housewife.

First Examination: Blood—Wassermann 4 plus. Spinal fluid—cells 26, globulin 1 plus, Wassermann 4 plus with 0.5 c.c., colloidal gold 4444433300.

Treatment—12 months: Silver Arsphenamine, 17; Mercurial, 24; Intraspinal, 9; Spinal drainages, 2.

Last Examination: Blood—Wassermann unchanged. Spinal fluid—cells 4, trace of globulin, Wassermann 4 plus with 1.0 c.c., and colloidal gold 1111110000.

There has been marked improvement.

CASE 10.—No. 40, B. L. Tabetic syndrome, male, age forty-one.

First Examination: Blood—Wassermann 4 plus. Spinal fluid—cells 10, globulin 1 plus, Wassermann 4 plus with 0.5 c.c., colloidal gold 5552555320.

Treatment—8½ months: Silver Arsphenamine, 22; Mercurial, 34; Intraspinal, 3.

Last Examination: Blood—Wassermann negative. Spinal fluid—no change except for a moderate reduction of the Wassermann reaction.

Symptomatic improvement was marked.

In this group of ten cases there was one questionable paretic, three tabetics, one case of optic atrophy and five cases of the meningovascular variety. One of the latter died with cerebral hemorrhage and the other three represent deep-seated pathology.

FORTY-EIGHT HOUR GROUP

This group comprised 46 specimens from 30 cases. Arsenic was present in an amount sufficient for quantitative determination in 60 per cent of the cases. The largest amount of arsenic was 74.6

mgm. per 100 gm. (For details see Case 3 of 24-hour group.) It is important to note that the same case (No. 28 A.S.) showed no arsenic in one specimen examined after a twenty-four hour interval.

Nine specimens from the same number of cases (30 per cent) showed no arsenic and three specimens from the same number of cases (10 per cent) showed but a trace. A classification and details of these cases follow:

DIAGNOSTIC CLASSIFICATION	ARSENIC ABSENT		ARSENIC PRESENT IN TRACE	
	FLUIDS	CASES	FLUIDS	CASES
Mesodermal (Cerebral)	0	0	1	1
Mesodermal (Cerebro-spinal)	1	1	1	1
Ectodermal (Paretic syndrome)	2	2		
Ectodermal (Tabetic syndrome)	4	4	1	1
Mixed (Cerebral)	1	1		
(Cerebro-spinal)	1	1		
Total	9	9	3	3
Case per cent	30		10	

ARSENIC ABSENT

Case 1.—No. 6, J. D. Cerebral mixed, male, age fifty-six, barber.

First Examination: Blood—Wassermann 4 plus. Spinal fluid—cells 33, globulin 2 plus, Wassermann 4 plus in 0.5 c.c., Vernes positive, colloidal gold 5555542211.

Treatment—10 months: Silver Arsphenamine, 18; Mercurial, 15; Intraspinal, 14.

Last Examination: Blood—Wassermann unchanged. Spinal fluid—cells 1 per cm., globulin 1 plus, Wassermann 4 plus in 0.5 c.c., colloidal gold 1111100000.

Death ensued from cerebral hemorrhage 13 months after the institution of treatment.

Case 2.—No. 17, 19, S. J. Cerebrospinal meningovascular, male, age thirty-six, shoemaker.

First Examination: Blood—Wassermann 4 plus. Spinal fluid—cells 193, globulin 3 plus, Wassermann 4 plus in 2.0 c.c., Vernes positive, colloidal gold 5555554210.

Treatment—11 months: Silver Arsphenamine, 31; Mercurial, 19; Intraspinal 15.

Last Examination: Blood—Wassermann negative. Spinal fluid—no cells, trace of globulin, Wassermann unchanged, colloidal gold 3222110000.

Clinically there was marked improvement.

Case 3.—No. 25, A. N. Cerebrospinal mixed, female, age thirty-five, housewife.

First Examination: Blood—Wassermann 4 plus. Spinal fluid—cells 10, globulin 2 plus, Wassermann 4 plus with 0.2 c.c., colloidal gold 5555431000.

Treatment—24 months: Arsphenamine, 27; Mercurial, 32; Intraspinal, 6.

Last Examination: Blood—Wassermann 2 plus. Spinal fluid—cells 8, trace of globulin, Wassermann negative with 2.0 c.c., colloidal gold 4333222100. Three months later after 7 Silver Arsphenamine injections the blood became negative.

Clinical improvement was marked.

CASE 4.—No. 27, T. P. Paretic syndrome, male, age fifty, clerk.

First Examination: Blood—Wassermann 4+. Spinal fluid—cells 20, globulin 1 plus, Wassermann 4 plus with 0.5 c.c., colloidal gold 5555554332.

Treatment—4 months: Silver Arsphenamine, 9; Mercurial, 15; Intraspinal, 2.

Last Examination: Blood—Wassermann unchanged. Spinal fluid—unchanged, reduction in cells to 0.

Death ensued a few months later.

CASE 5.—No. 29, A. S. The same as Case 3 of the 24 hour group. This case illustrated a striking difference in permeability for arsenic having, as noted above, the largest amount encountered among the 48 hour specimens but on two other occasions none.

CASE 6.—No. 31, N. A. Tabetic syndrome, male, age forty-seven, watchman.

First Examination: Blood—Wassermann doubtful, Vernes negative. Spinal fluid—cells 8, globulin 1 plus, Wassermann negative with 2.0 c.c., Vernes positive, colloidal gold 4332110000.

Treatment—12 months: Silver Arsphenamine, 23; Mercurial, 15; Intraspinal, 12; Spinal drainage, 1.

Last Examination: Blood—Wassermann essentially unchanged. Spinal fluid—was essentially unchanged.

Clinical improvement was noted.

CASE 7.—No. 32, E. G. Tabetic syndrome, male, age thirty-seven, operator.

First Examination: Blood—Wassermann 1 plus. Spinal fluid—cells 54, globulin 4 plus, Wassermann 4 plus with 0.2 c.c., colloidal gold 5555431000.

Treatment—42 months: Arsphenamine, 11; Silver arsphenamine, 1; Mercurial, 52; Intraspinal, 2.

Last Examination: Blood—Wassermann negative. Spinal fluid—negative.

The clinical symptoms indicated arrest.

Before the examination of this fluid for arsenic no arsphenamine, with the exception of the one injection, had been administered for nearly two years.

CASE 8.—No. 36, L. P. Tabetic syndrome, male, age forty-one, salesman.

First Examination: Blood—Wassermann 4 plus. Spinal fluid—cells 20, globulin 2 plus, Wassermann 2 plus with 0.2 c.c., colloidal gold 5555443000.

Treatment—48 months: Arsphenamine, 30; Silver Arsphenamine, 41; Mercurial, 119; Intraspinal, 32; Spinal drainage, 9.

Last Examination: Blood—Wassermann 2 plus. Spinal fluid—cell 1, globulin 1 plus, Wassermann 4 plus with 1.0 c.c., colloidal gold 5555555432.

Clinically there has been great improvement and apparent arrest in this case. The serology warns against hopeful prognosis. It is our belief that only by virtue of the persistent treatment has the activity of the spirochetes been controlled.

CASE 9.—No. 46, J. T. See No. 9 of two hour group.

ARSENIC PRESENT IN TRACE

CASE 10.—No. 2, G. H. Cerebral meningeal, male, age 23, auto mechanic.

First Examination: Blood—Wassermann negative. Spinal fluid—cells 16, globulin 1 plus, Wassermann 3 plus with 1.0 c.c., colloidal gold 2222311100.

Treatment—18 months: Arsphenamine, 5; Silver Arsphenamine, 23; Mercurial, 27; Intraspinal, 5; Spinal drainage, 3.

Last Examination: Blood—Wassermann 3 plus. Spinal fluid—cell 1, globulin normal, Wassermann negative in 2.0 c.c., negative Vernes, colloidal gold 1111100000.

The clinical symptoms were greatly improved and there was an apparent arrest but after three months' discontinuance of therapy at the patient's volition symptoms recurred and the spinal fluid again became positive.

CASE 11.—No. 9, S. W. Cerebral meningovascular, male, age thirty-three, clerk.

First Examination: Blood—Wassermann 4 plus. Spinal fluid—cells 13, two plus globulin, Wassermann positive with 0.5 c.c., colloidal gold 5555555220.

Treatment—9 months: Silver Arsphenamine, 21; Mercurial, 20; Intraspinal, 7.

Last Examination: Blood—Wassermann 1 plus. Spinal fluid—unchanged except for a diminution in cells to 4.

CASE 12.—No. 35, L. O. Tabetic syndrome, male, age forty-five, chef.

First Examination: Blood—Wassermann 3 plus. Spinal fluid—cells 7, trace of globulin, Wassermann positive with 0.5 c.c., colloidal gold 3332100000.

Treatment—7 months: Silver Arsphenamine, 16; Mercurial injections, 8; Intraspinal, 3.

The serology is still positive but subjective and objective clinical improvement has been noted.

CASE 13.—No. 37, L. P. Same as Case 8 of this group.

SEVENTY-TWO HOUR GROUP

The group consisted of 33 specimens from 25 cases. Arsenic was present in an amount sufficient for quantitative determination in 68 per cent of the cases. The largest quantity of arsenic was 192 mgm. per 100 gm. This came from a case of cerebral meningeal syphilis. The neurologic symptoms originated after one year of intensive intravenous therapy. The blood Wassermann had become negative and during a rest period the symptoms which consisted chiefly in continuous excruciating headache originated. The only physical signs were dilated pupils and hyperreflexia. The blood Wassermann and Vernes reactions were negative. In the spinal fluid there were 541 cells, two plus globulin, Wassermann four plus with 0.5 c.c. colloidal gold 3334455311.

After three months of treatment consisting of 10 silver arsphenamine, 10 mercurial, 3 intraspinal injections and two spinal drainages, the spinal fluid became negative and there was complete relief of all symptoms. Six months later the serology was still negative and the clinical condition was still good.

Six specimens (24 per cent) showed no arsenic and two specimens (8 per cent) showed only a trace. The classification and details of these cases follow:

DIAGNOSTIC CLASSIFICATION	ARSENIC ABSENT		ARSENIC PRESENT IN TRACE	
	FLUIDS	CASES	FLUIDS	CASES
Mesodermal (Cerebral)	2	2	1	1
Mesodermal (Cerebrospinal)	2	2	1	1
Ectodermal (Tabetic syndrome)	2	2	0	0
Total	6	6	2	2
Case per cent	24		8	

Case 1.—No. 4, A. B. See Case 10 in 2 hour group.

Case 2.—No. 8, D. F. Cerebral meningovascular with bilateral optic atrophy, female, age forty-three, housewife.

First Examination: Blood—Wassermann negative. Spinal fluid—cells 3, globulin 1 plus, Wassermann 4 plus in 0.5 c.c., Vernes positive, colloidal gold 5533211000.

Treatment—9 months: Silver Arsphenamine, 22; Mercurial, 12; Intraspinal, 13.

Last Examination: Spinal fluid—negative except the colloidal gold 3345543210.

The visual acuity remained stationary.

Case 3.—No. 15, J. S. See Case No. 2 in 48 hour group.

Case 4.—No. 16, E. R.—Cerebrospinal meningovascular, female, age forty, dressmaker.

First Examination: Blood—Wassermann 4 plus. Spinal fluid—cells 20, globulin trace, Wassermann 4 plus with 0.5 c.c., colloidal gold 5555221111.

Treatment—12 months: Silver Arsphenamine, 17; Mercurial, 16; Intraspinal, 8.

Last Examination: Blood—Wassermann negative. Spinal fluid—no cells, globulin normal, Wassermann 2 plus with 2.0 c.c., colloidal gold 5434321000.

There was decided clinical improvement.

Case 5.—No. 20, M. F. Tabetic syndrome, female, age forty-seven, housewife.

First Examination: Blood—Wassermann 2 plus. Spinal fluid—cells 10, globulin trace, Wassermann 4 plus in 0.5 c.c., Vernes positive, colloidal gold 5554543210.

Treatment—17 months: Arsphenamine, 5; Silver Arsphenamine, 16; Mercurial, 34; Intraspinal, 8; Spinal drainage, 1.

Last Examination: Blood—Wassermann negative. Spinal fluid—negative.

There was a complete arrest of progress.

Case 6.—No. 33, L. O. Tabetic syndrome, male, age forty-five, chef.

First Examination: Blood—Wassermann 3 plus. Spinal fluid—cells 7, trace globulin, Wassermann positive with 0.5 c.c., colloidal gold 3332100000.

Treatment—7 months: Silver Arsphenamine, 16; Mercurial, 8; Intraspinal, 3.

The serology is still positive but subjective and objective clinical improvement has been noted.

ARSENIC PRESENT IN TRACE

Case 7.—No. 7, P. P. Cerebral meningovascular, male, age thirty-eight, driver.

First Examination: Blood—Wassermann 1 plus. Spinal fluid—cells 66, 2 plus globulin, Wassermann 4 plus with 2.0 c.c., colloidal gold 5555555551.

Treatment—12 months: Arsphenamine, 10; Silver Arsphenamine, 21; Mercurial, 6; Intraspinal, 1; Spinal Drainage, 3.

Last Examination: Blood—Wassermann negative. Spinal fluid—negative.

There was clinical evidence of pathologic arrest.

Case 8.—No. 13, C. B. Same as Case 5 in 24 hour group.

In this group of eight cases showing no arsenic or only a trace at the end of seventy-two hours includes two cases of optic atrophy, two tabetics and four cases of deep seated lesions of the meningovascular type.

CONCLUSIONS

From a review of our results which include the examination of 239 spinal fluids taken from 151 patients after the intravenous administration of silver arsphenamine, we infer the following facts to be proved:

1. Arsenic passes into the spinal fluid.

2. Arsenic can be found in the spinal fluid at the end of two hours in an amount as large as 143 mgm. per 100 gm. of dried specimen.

3. Arsenic can be found in the spinal fluid as late as seventy-two hours in an amount as large as 192 mgm. per 100 gm. of dried specimen.

4. In general the arsenic content in the spinal fluid falls after the first two hours. It rises slightly between twenty-four and forty-eight hours and at the end of seventy-two hours is present in greater quantity than at any time between two and seventy-two hours. This statement is applicable only in the abstract and does not hold true equally for all types of neurosyphilis. This point together with additional analytical features of the results will be discussed in a later publication.

TABLE I

TWO HOUR GROUP

	PATIENT SERIAL NO.	DATE OF LAST INJECTION	NO. PREVIOUS INJECTIONS	DRUG USED	DOSE	TIME AFTER INJECTION	METHOD TREATMENT	WT. OF SPECIMEN		PER CENT SOLIDS	AS IN MG. PER 100 GR. SPEC.	RACE SEX	AGE OCCUPATION	BLOOD W. R.	CELLS	GLOB.	WASSERMANN (VERNES)	COLLOIDAL GOLD	CLASSIFICATION	
								MOIST	DRY											
1	183	3/ 7/21	1	S.A.	0.1	2 hr.	Drainage	6.4959	0.0788	1.21	17.7	W. M.	26 Chauffeur	+	541	++	++++ in 0.5 c.c.	3334455310	Cerebral meningeal. Acute syphilitic meningitis of the convexity. Extreme cephalalgia. Anxiety psychoneurosis	1
2	191	3/16/21	3 4 Hg	S.A.	0.1	2 hr.	Drainage	5.0306	0.0546	1.08	18.3	W. M.	26 Chauffeur	+	133	+++	Not done	5554433210	Cerebral meningeal. Acute syphilitic meningitis of the convexity. Extreme cephalalgia. Anxiety psychoneurosis	2
3	261	4/ 4/21	6 6 Hg	S.A.	0.2	2 hr.	Drainage	5.3808	0.0588	1.08	20.4	W. M.	26 Chauffeur	+	59	+	++++ in 2 c.c. V 7.5	5554443321	Cerebral meningeal. Acute syphilitic meningitis of the convexity. Extreme cephalalgia. Anxiety psychoneurosis	3
4	184	3/ 9/21	19 Arsph. 1 S.A. 44 Hg	S.A.		2 hr.	Drainage	4.5720	0.0490	1.07	29.0	W. M.	26 Plasterer	++++	18	+	++++ in 0.5 c.c. V 5.5	4445554321	Cerebral meningeal. Subacute syphilitic meningitis of the convexity. Cephalalgia. Anxiety psychoneurosis	4
5	26	1/26/21	5 Arsph. 3 S.A.	S.A.	0.1	2 hr.	Drainage	5.4202	0.0572	1.06	4.3	W. M.	23 Auto Mechanic	?	12	Neg.	Neg. in 2 c.c.	1233310000	Cerebral meningeal. Subacute cerebral meningitis of the convexity. Epileptiform seizures	5
6	97	2/ 9/21	9	S.A.	0.1	2 hr.	S.E.+ 1/5	5.8821	0.0590	1.003	0.84	W. M.	23 Auto Mechanic	+	Neg.	Neg.	Neg. in 2 c.c. V 6.5	4445421000	Cerebral meningeal. Subacute cerebral, etc.	6
7	287	4/ 8/21	12	S.A.	0.2	2 hr.	Drainage	6.8593	0.0700	1.16	5.7	W. M.	23 Auto Mechanic	?	37	Neg.	+++ in 2 c.c. V 0.5	1223222000	Cerebral meningeal. Subacute cerebral, etc.	7
8	133	2/ 7/21	8-4 S.A. 10 Hg	S.A.	0.1	2 hr.	Drainage	6.4266	0.0794	1.23	3.7	W. M.	35 Barber	++++	9	++	Neg. in 1 c.c. V 7.5	0122333431	Cerebral meningeal. Subacute cerebral meningitis of the convexity. Epileptiform seizures	8
9	293	4/ 6/21	12 15 Hg	S.A.	0.2	2 hr.	Drainage	5.7105	0.0682	1.19	14.0	W. M.	35 Barber	++++	3	+	+ ? in 2 c.c.	1123332221	Cerebral meningeal. Subacute cerebral meningitis of the convexity. Epileptiform seizures	9
10	412	5/23/21	19 15 Hg	S.A.	0.2	2 hr.	Drainage	5.5660	0.0660	1.18	10.6	W. M.	35 Barber	++++	1	++	+ ? in 2 c.c. V 7.5	4444411111	Cerebral meningeal. Subacute cerebral meningitis of the convexity. Epileptiform seizures	10
11	126	2/16/21	5	S.A.	0.1	2 hr.	Drainage	6.1714	0.0650	1.05	50.0	W. M.	36 Laborer	++++	1	Neg.	Neg. in 2 c.c. V 7	2233331000	Cerebral vascular. Right hemiparesis	11
12	188	3/ 4/21	6 15 Hg	S.A.	0.1	2 hr.	Drainage	3.8886	0.0405	1.04	14.7	W. M.	36 Laborer	++++	1	+	Neg. in 2 c.c.	———	Cerebral vascular. Right hemiparesis	12
13	432	6/ 8/21	7 Arsph. 13 S.A. 32 Hg Back to 1919	S.A.	0.2	2 hr.	Drainage	4.5369	0.0487	1.07	10.0	W. M.	48 Guilder	Neg.	3	Neg.	Neg. in 2 c.c.	1110000000	Cerebral vascular with secondary parenchymatous degeneration. Syphilitic spastic triplegia	13
14	130	2/14/21	9 1 S.A.	S.A.	0.2	2 hr.	S.E. + 1/10	5.8059	0.0629	1.08	3.1	W. M.	61 Salesman	+ ?	1	+	+ in 1 c.c. V 7	5555541000	Cerebral vascular with secondary parenchymatous degeneration. Weber's syndrome	14
15	35	1/28/21	6-4 Arsph. 2 S.A. 2 Hg	S.A.	0.1	2 hr.	Drainage	6.5010	0.0710	1.09	2.8	W. M.	56 Janitor	Neg.	7	+	++++ in 1 c.c. V ½	5555432100	Cerebral vascular with secondary parenchymatous changes. Hemiplegia	15

Table I—Cont'd

16	185	3/ 9/21	8 10 Hg	S.A.	0.1	2 hr.	L.P.	5.3754	0.0618	1.11	11.3	W. M.	55 Laborer	Neg.	20	+	Neg. in 2 c.c. V 7.5	1122210000	Cerebral vascular. Endarteritis	16
17	122	2/20/21	57	S.A.	0.2	24 hr.	I.V. and S. E.	4.3830	0.0477	1.08	12.6	W. F.	54	Neg.	19	Trace	Neg. in 2 c.c.	4554321000	Cerebral meningovascular. Chronic syphilitic basilar meningitis. Paresis of left III and VIII nerves	17
18	50	2/ 2/21	7-5 Arsph. 2 S.A.	S.A.	0.1	2 hr.	Drainage	7.5578	0.0828	1.09	10.9	W. M.	60 Tailor	++++	5	Neg.	++++ in 2 c.c. V 7.5	0111100000	Cerebral meningovascular. Chronic syphilitic basilar meningitis. Ophthalmoplegia in distribution of right III and IV nerves	18
19	475	6/27/21	5 15 Hg	S.A.	0.2	2 hr.	Drainage	6.3378	0.0671	1.05	0.74	W. M.	36 Fireman	++	1	Neg.	Neg. in 2 c.c. V 0	0000000000	Cerebral meningovascular. Cephalalgia. Anxiety psychoneurosis	19
20	27	1/26/21	5-2 Arsph. 3 S.A. 3 Hg	S.A.	0.1	2 hr.	Drainage	6.3412	0.0620	0.98	0.8	W. F.	24 Hairdresser	++++	1	Trace	? in 2 c.c.	1233100000	Cerebral meningovascular. Organically asymptomatic	20
21	533	7/13/21	8-4 Arsph. 4 S.A. 25 Hg	S.A.	0.2	2 hr.	Drainage	6.2031	0.0719	1.15	Trace	W. M.	37 Salesman	+	3	Trace	? in 2 c.c.	5555444221	Cerebral meningovascular. Anxiety psychoneurosis. Early optic atrophy	21
22	434	6/ 8/21	7-6 S.A. 15 Hg	S.A.	0.2	2 hr.	Drainage	4.7962	0.0486	1.01	6.1	W. M.	56 Jeweler	++++	28	Trace	++++ in 2 c.c. V 6	2211100000	Cerebral meningovascular. Manic depressive psychosis	22
23	581	7/27/21	13	S.A.	0.2	2 hr.	Drainage	8.1740	0.0870	1.06	6.9	W. M.	56 Jeweler	+	58	+	Neg. in 2 c.c. V 8	4433321000	Cerebral meningovascular. Manic depressive psychosis	23
24	96	2/ 9/21	12-2 S.A. 10 Hg	S.A.	0.1	2 hr.	Drainage	5.3169	0.0544	1.02	25.0	W. M.	38 Driver	Neg.	2	Neg.	Neg. in 1 c.c. V 5.5	3334310000	Cerebral meningovascular. Anxiety psychoneurosis with conversion symptoms	24
25	147	2/28/21	26-5 S.A. 1 Hg	S.A.	0.2	2 hr.	Drainage	4.9895	0.0526	1.05	18.9	W. M.	52 Laborer	++	13	+	++++ in 1 c.c. V 6.5	5533331100	Cerebral meningovascular. Trigeminal neuralgia	25
26	410	5/20/21	22 Arsph. 1 S.A. 30 Hg	S.A.	0.2	2 hr.	Drainage	5.7857	0.0569	0.98	3.51	W. M.	37 Painter	+	1	Neg.	+ in 2 c.c. V 6	4442221110	Cerebral meningovascular. Ophthalmoplegia left third	26
27	483	6/20/21	22 Arsph. 2 S. A.	S.A.	0.2	2 hr.	Drainage	3.3968	0.0409	1.20	8.53	W. M.	37 Painter	Neg.	3	Trace	+ in 2 c.c. V 6	2222111000	Cerebral meningovascular. Ophthalmoplegia left third	27
28	42	1/31/21	10-4 Arsph. 6 S.A.	S.A.	0.1	2 hr.	Drainage	3.4221	0.0405	1.18	2.4	C. M.	37 Laborer	++++	Neg.	Neg.	Neg. in 2 c.c.	1110000000	Spinal meningovascular. Amyotrophy of right shoulder girdle and arm	28
29	251	3/23/21	8-2 Arsph. 6 S.A.	S.A.	0.2	2 hr.	Drainage	7.8745	0.0837	1.06	143.0	W. M.	40 Watchman	++++	9	+	++++ in 2 c.c. V 5.5	5554433220	Spinalmeningovascular. Chronic hypertrophic syphilitic cervical meningitis. Amyotrophy	29
30	49	2/ 2/21	13-11 Arsph. 2 S.A.	S.A.	0.1	2 hr.	Drainage	5.8640	0.0742	1.28	2.6	C. M.	60 Butler	++++	30	++	++++ in 2 c.c. V 7	5555552221	Spinal meningovascular. Amyotrophy	30
31	149	2/28/21	14 S.A. 15 Hg	S.A.	0.2	2 hr.	Drainage	4.6512	0.0653	1.40	0.76	C. M.	60 Butler	++++	16	++	++++ in 1 c.c. V 7	———	Spinal meningovascular. Amyotrophy	31
32	190	3/16/21	15	S.A.	0.1	2 hr.	Drainage	6.7414	0.0870	1.29	2.8	C. M.	60 Butler	+++	12	++	++++ in 2 c.c. V 7.5	5555444431	Spinal meningovascular. Amyotrophy	32
33	316	4/13/21	18 S.A.	S.A.	0.2	2 hr.	Drainage	4.9715	0.0586	1.17	Lost	C. M.	60 Butler	+++	8	++	++++ in 0.5 c.c. V 4	5555555322	Spinal meningovascular. Amyotrophy	33
34	120	3/ 1/21	15-8 Arsph. 7 S.A.	S.A.	0.2	2 hr.	Drainage	4.5180	0.0500	1.10	16.0	W. M.	42 Fireman	++++	7	+	++++ in 0.5 c.c. V Neg.	5533322322	Cerebrospinal meningovascular	34
35	348	4/29/21	18 30 Hg	S.A.	0.2	2 hr.	Drainage	4.1916	0.0389	0.92	1.29	W. M.	42 Fireman	++++	7	+	++++ in 2 c.c. V Neg.	2224442222	Cerebrospinal meningovascular	35

TABLE I—CONT'D

	PATIENT SERIAL NO.	DATE OF LAST INJECTION	NO. PREVIOUS INJECTIONS	DRUG USED	DOSE	TIME AFTER INJECTION	METHOD TREATMENT	WT. OF SPECIMEN		PER CENT SOLIDS	AS IN MG. PER 100 GR. SPEC.	RACE SEX	AGE OCCUPATION	BLOOD W. R.	CELLS	GLOB.	WASSERMANN (VERNES)	COLLOIDAL GOLD	CLASSIFICATION	
								MOIST	DRY											
36	129	2/14/21	3 10 Hg	S.A.	0.1	2 hr.	Drainage	5.9112	0.0620	1.04	1.6	W. F.	44 Housewife	++++	11	+	Neg. in 1 c.c. V 6	5544543100	Cerebrospinal miningovascular	36
37	377	5/ 6/21	8	S.A.	0.2	2 hr.	Drainage	4.8130	0.0503	1.04	26.5	W. F.	44 Housewife	++++	1	Neg.	Neg. in 2 c.c. V 7.5	2221100000	Cerebrospinal meningovascular	37
38	259	4/ 4/21	39-38 Arsph. 1 S.A.	S.A.	0.2	2 hr.	Drainage	7.2590	0.0775	1.06	4.5	W. M.	39 Laborer	Neg.	4	Neg.	Neg. in 2 c.c. V 7	2221110000	Cerebrospinal meningovascular	38
39	166	2/ 4/21	1	S.A.	0.1	2 hr.	Drainage	3.5922	0.0352	0.97	17.0	W. F.	38 Housewife	++++	1	Neg.	++++ in 2 c.c. V 5.5.	2333210000	Cerebrospinal meningovascular	39
40	295	4/ 1/21	2	S.A.	0.2	2 hr.	Drainage	3.6886	0.0321	0.88	3.1	W. F.	38 Housewife	++++	Neg.	Trace	? in 2 c.c. V 5.5	3333221100	Cerebrospinal meningovascular	40
41	349	4/25/21	3 5 Hg	S.A.	0.2	2 hr.	Drainage	4.4702	0.0433	0.96	4.1	W. F.	38 Housewife	++++	Neg.	Neg.	++++ in 2 c.c. V 7	5442211000	Cerebrospinal meningovascular	41
42	493	7/ 6/21	26 1 S.A.	S.A.	0.2	2 hr.	Drainage	4.1518	0.0488	1.17	47.7	W. F.	38 Maid	+	3	Neg.	Neg. in 2 c.c. V 6	———	Cerebrospinal meningovascular	42
43	41	1/31/21	27 1 S.A. 15 Hg	S.A.	0.2	2 hr.	Drainage	5.9059	0.0671	1.13	8.9	W. F.	34 Housewife	+++	7	Neg.	++++ in 2 c.c. V 8	1223220000	Cerebrospinal meningovascular	43
44	146	3/ 2/21	22 8 S.A. 20 Hg	S.A.	0.2	2 hr.	Drainage	3.9130	0.0397	1.01	25.1	W. M.	42 Packer	+	1	Trace	Neg. in 2 c.c. V 6.5	4433321000	Cerebrospinal meningovascular	44
45	260	4/ 4/21	23 25 Hg	S.A.	0.2	2 hr.	Drainage	5.8815	0.0635	1.07	62.9	W. M.	42 Packer	+	3	Trace	+++ in 2 c.c.	4444333211	Cerebrospinal meningovascular	45
46	350	4/27/21	27	S.A.	0.2	2 hr.	Drainage	4.0360	0.0377	0.93	6.63	W. M.	42 Packer	Neg.	1	Neg.	+++ in 2 c.c. V Neg.	4522110000	Cerebrospinal meningovascular	46
47	431	6/ 8/21	29 30 Hg	S.A.	0.2	2 hr.	Drainage	2.7053	0.0292	1.07	Trace	W. M.	42 Packer	Neg.	3	Trace	++++ in 2 c.c. V 4	1110000000	Cerebrospinal meningovascular	47
48	495	7/ 6/21	30 31 Hg	S.A.	0.2	2 hr.	Drainage	4.8140	0.0534	1.10	Trace	W. M.	42 Packer	Neg.	1	+	Neg. in 2 c.c. C ++++ in 2 c.c. A V Neg.	Not done	Cerebrospinal meningovascular	48
49	391	5/11/21	9 17 Hg	S.A.	0.2	2 hr.	Drainage	3.9474	0.0379	0.96	5.2	W. M.	58 Salesman	++++	Neg.	Neg.	Neg. in 2 c.c. V 3.5	1100000000	Cerebrospinal meningovascular	49
50	372	5/ 6/21	23 1 S.A.	S.A.	0.2	2 hr.	Drainage	6.0207	0.0656	1.08	0	W. M.	57 Painter	++++	17	+	++++ in 1 c.c. V 4	2222111000	Cerebrospinal mixed. Bilateral optic atrophy, extreme	50
51	536	7/12/21	24	S.A.	0.2	2 hr.	Drainage	4.9738	0.0584	1.17	0	W. M.	57 Painter	++++	5	Trace	++++ in 1 c.c. V 3	4222111110	Cerebrospinal mixed. Bilateral optic atrophy, extreme	51
52	145	3/ 2/21	2 5 Hg	S.A.	0.2	2 hr.	Drainage	5.0614	0.0522	1.03	3.8	C. M.	48 Porter	++++	13	+	Neg. in 2 c.c. V 6	2211000000	Cerebrospinal mixed. Bilateral optic atrophy, moderate degree	52
53	253	3/20/21	4 7 Hg	S.A.	0.2	2 hr.	Drainage	4.6406	0.0476	1.02	42.01	C. M.	48 Porter	++++	15	+	++++ in 2 c.c. V 0.5	2221100000	Cerebrospinal mixed. Bilateral optic atrophy, moderate degree	53
54	371	5/ 2/21	9 10 Hg	S.A.	0.2	2 hr.	Drainage	6.7952	0.0705	1.03	Trace	C. M.	48 Porter	++++	8	Neg.	++++ in 2 c.c. V 1	2211100000	Cerebrospinal mixed. Bilateral optic atrophy, moderate degree	54
55	416	6/ 1/21	10 10 Hg	S.A.	0.2	2 hr.	Drainage	6.5136	0.0662	1.01	0	C. M.	48 Porter	++++	33	+	++++ in 1 c.c. V 4	2222111000	Cerebrospinal mixed. Bilateral optic atrophy, moderate degree	55

TABLE I—Cont'd

56	499	6/29/21	11	S.A.	0.2	2 hr.	Drainage	4.8205	0.0571	1.18	0	C. M.	48 Porter	++++	24	+	++++ in 1 c.c. V 7	2222000000	Cerebrospinal mixed. Bilateral optic atrophy, moderate degree	56
57	576	7/25/21	12	S.A.	0.2	2 hr.	Drainage	5.1302	0.0512	0.99	46.6	C. M.	48 Porter	++++	24	+	++++ in 1 c.c. V 7	2222000000	Cerebrospinal mixed. Bilateral optic atrophy, moderate degree	57
58	121	2/18/21	11 2 S.A. 15 Hg	S.A.	0.1	2 hr.	Drainage	5.5664	0.0618	1.09	12.9	W. M.	42 Peddler	++++	1	Trace	++ in 2 c.c. V 4	1223333100	Cerebrospinal mixed. Bilateral optic atrophy with extreme exophthalmos	58
59	234	3/21/21	12	S.A.	0.2	2 hr.	Drainage	7.1705	0.0797	1.11	1.25	W. M.	42 Peddler	++++	13	Trace	++ in 2 c.c. V 4.5	0122221000	Cerebrospinal mixed. Bilateral optic atrophy with extreme exophthalmos	59
60	1717	4/26/22	92 15 S.A.	S.A.	0.2	2 hr.	Drainage	4.2419	0.0415	0.97	12.0	W. M.	45 Peddler	+	Neg.	Neg.	Neg. in 2 c.c.	2222111000	Cerebrospinal mixed. Bilateral optic atrophy, extreme	60
61	529	7/20/21	10 2 S.A.	S.A.	0.1	1½ hr.	Drainage	4.7124	0.0557	1.18	0	W. M.	32 Clerk	++++	8	+	++++ in 0.5 c.c. V Neg.	5555542100	Cerebral parenchymatous. Paretic syndrome	61
62	480	6/22/21	7 9 Hg	S.A.	0.2	2 hr.	Drainage	4.0364	0.0455	1.12	0	W. M.	47 Actor, Dead	+++	1	++	++++ in 1 c.c.	5555321100	Cerebral parenchymatous. Paretic syndrome	62
63	528	7/20/21	12	S.A.	0.2	2 hr.	Drainage	3.7098	0.0451	1.24	0	W. M.	47 Actor, Dead	. .	7	++	++++ in 1 c.c.	5555544111	Cerebral parenchymatous. Paretic syndrome	63
64	125	2/16/21	4 1 Hg	S.A.	0.1	2 hr.	Drainage	6.4743	0.0698	1.07	3.59	W. M.	35 Factory Worker	++++	12	+++	++++ in 0.5 c.c. V 1	5555554321	Cerebral parenchymatous. Paretic syndrome	64
65	161	2/ 7/21	7 4 S.A. 9 Hg	S.A.	0.1	2 hr.	Drainage	4.5875	0.0550	1.19	65.0	W. M.	56 Actor, Dead	++++	9	+	++++ in 1 c.c.	1142332100	Spinal parenchymatous. Tabetic syndrome	65
66	192	3/16/21	0 10 Hg	S.A.	0.2	2 hr.	Drainage	5.7837	0.0627	1.08	25.5	W. F.	35 Housewife	++++	8	+	++++ in 2 c.c. V 4	3433333210	Spinal parenchymatous. Tabetic syndrome	66
67	411	5/16/21	11-3 Arsph. 8 S.A. 16 Hg	S.A.	0.1	2 hr.	Drainage	4.3410	0.0445	1.02	Trace	W. F.	34 Housewife	+ in A	65	+	++++ in 1 c.c. V 8	5542221111	Spinal parenchymatous. Tabetic syndrome	67
68	417	6/ 1/21	12	S.A.	0.15	2 hr.	Drainage	5.6046	0.0585	1.04	Trace	W. F.	34 Housewife	. .	39	Trace	++++ in 2 c.c. V 5.5	4422211111	Spinal parenchymatous. Tabetic syndrome	68
69	537	7/12/21	16	S.A.	0.15	2 hr.	Drainage	5.0979	0.0521	1.02	6.2	W. F.	34 Housewife	+++	45	+	Neg. in 2 c.c. V 7	2211111000	Spinal parenchymatous. Tabetic syndrome	69
70	430	6/ 3/21	10-5 Arsph. 5 S.A. 10 Hg	S.A.	0.2	2 hr.	Drainage	6.6413	0.0691	1.04	0.72	W. F.	47 Housewife	+++	Neg.	Neg.	Neg. in 2 c.c. V 7	1111000000	Spinal parenchymatous. Tabetic syndrome	70
71	187	3/ 4/21	7 15 Hg	S.A.	0.1	2 hr.	Drainage	3.9050	0.0413	1.05	33.9	W. F.	45 Seamstress	+	3	+	Neg. in 2 c.c. V 8	4333210000	Spinal parenchymatous. Tabetic syndrome	71
72	285	4/ 8/21	10	S.A.	0.2	2 hr.	Drainage	12.1440	0.1407	1.15	1.3	W. F.	45 Seamstress	Neg.	1	Neg.	Neg. V 6	5543322111	Spinal parenchymatous. Tabetic syndrome	72
73	397	5/18/21	14	S.A.	0.2	2 hr.	Drainage	4.6885	0.0492	1.04	5.4	W. F.	45 Seamstress	Neg.	4	Neg.	++++ in 2 c.c. V 6	4442221100	Spinal parenchymatous. Tabetic syndrome	73
74	132	2/14/21	10-6 Arsph. 4 S.A. 17 Hg	S.A.	0.1	2 hr.	Drainage	4.6406	0.0481	1.03	12.4	W. F.	29 Housewife	++++	7	Trace	Neg. in 1 c.c. V 7.5	5555443210	Spinal parenchymatous. Tabetic syndrome with right optic atrophy	74
75	291	4/ 1/21	13-5 Arsph. 8 S.A. 20 Hg	S.A.	0.2	2 hr.	Drainage	6.8255	0.0673	0.98	Trace	W. M.	41 Mechanic	++++	3	Trace	+++ in 2 c.c.	——	Spinal parenchymatous. Tabetic syndrome	75
76	323	4/15/21	14	S.A.	0.2	2 hr.	Drainage	6.7494	0.0574	0.85	0.87	W. M.	41 Mechanic	++++	1	Trace	+++ in 2 c.c. V 5.5.	5544433220	Spinal parenchymatous. Tabetic syndrome	76
77	395	5/20/21	16	S.A.	0.2	2 hr.	Drainage	6.4636	0.0686	1.06	0	W. M.	41 Mechanic	++++	2	Trace	++++ in 2 c.c. V 4	5555442211	Spinal parenchymatous. Tabetic syndrome	77

TABLE I

TWO HOUR GROUP

	PATIENT SERIAL NO.	DATE OF LAST INJECTION	NO. PREVIOUS INJECTIONS	DRUG USED	DOSE	TIME AFTER INJECTION	METHOD TREATMENT	WT. OF SPECIMEN		PER CENT SOLIDS	AS IN MG. PER 100 GR. SPEC.	RACE SEX	AGE OCCUPATION	BLOOD W. R.	CELLS	GLOB.	WASSERMANN (VERNES)	COLLOIDAL GOLD	CLASSIFICATION	
								MOIST	DRY											
78	451	6/ 9/21	17	S.A.	0.2	2 hr.	Drainage	4.9429	0.0565	1.14	0	W. M.	41 Mechanic	++++	1	Trace	++++ in 2 c.c. V 4	4422111000	Spinal parenchymatous. Tabetic syndrome	78
79	1	1/24/21	7-6 Arsph. 1 S.A. 15 Hg	S.A.	0.1	2 hr.	Drainage	7.9261	0.0759	0.96	5.2	W. F.	30 Stenographer	++++	7	Neg.	++++ in 2 c.c. V 5.5	4453332000	Spinal parenchymatous. Tabetic syndrome	79
80	180	2/25/21	10-8 Arsph. 2 S.A.	S.A.	0.1	2 hr.	Drainage	4.6210	0.0447	0.98	53.7	W. F.	45 Housewife	++++	3	Trace	Neg. in 2 c.c. V 8	2233420000	Spinal parenchymatous. Tabetic syndrome	80
81	335	4/20/21	12 15 Hg	S.A.	0.2	2 hr.	Drainage	4.1839	0.0429	1.02	5.8	W. F.	45 Housewife	++++	3	Trace	Neg. in 2 c.c. V 6.5	2233220000	Spinal parenchymatous. Tabetic syndrome	81
82	469	6/15/21	6 1 Hg	S.A.	0.2	2 hr.	Drainage	3.9606	0.0399	1.007	2.5	W. M.	46 Tailor	+++	3	Trace	+++ in 2 c.c. V 8	1110000000	Spinal parenchymatous. Tabetic syndrome	82
83	577	7/25/21	9	S.A.	0.2	2 hr.	Drainage	5.2535	0.0482	0.91	0	W. M.	46 Tailor	Neg.	Neg.	Neg.	Neg. in 2 c.c. V 8	2110000000	Spinal parenchymatous. Tabetic syndrome	83
84	127	2/16/21	14 3 Hg	S.A.	0.1	2 hr.	Drainage	6.6741	0.0643	0.96	9.3	W. F.	45 Housewife	++	3	+	++ in 2 c.c. V 7	4443331000	Spinal parenchymatous. Tabetic syndrome	84
85	534	7/11/21	1 15 Hg	S.A.	0.2	2 hr.	Drainage	5.6060	0.0684	1.22	4.3	W. M.	45 Laborer	++++	27	++	++++ in 2 c.c. V 7	5555211100	Spinal parenchymatous. Tabetic syndrome	85
86	409	5/11/21	8	S.A.	0.2	2 hr.	Drainage	5.4902	0.0595	1.08	4.2	W. M.	56 Bookkeeper	++	20	+	Neg. in 2 c.c. V 1	2222111100	Spinal parenchymatous. Tabetic syndrome	86
87	415	6/ 1/21	9	S.A.	0.2	2 hr.	Drainage	6.0386	0.0538	0.88	0	W. M.	56 Bookkeeper	Neg.	48	++	++++ in 0.5 c.c. V 4.5	5555522222	Spinal parenchymatous. Tabetic syndrome	87
88	474	6/27/21	10	S.A.	0.2	2 hr.	Drainage	4.6040	0.0578	1.25	5.1	W. M.	56 Bookkeeper	Neg.	7	+	++ in 1 c.c. V Neg.	4441100000	Spinal parenchymatous. Tabetic syndrome	88
89	2	1/26/21	1 5 Hg	S.A.	0.1	2 hr.	Drainage	5.3227	0.0565	1.06	3.5	W. M.	50 Tailor	Neg.	40	+	++++ in 2 c.c.	5555544433	Spinal parenchymatous. Tabetic syndrome	89
90	128	2/16/21	3 5 Hg	S.A.	0.1	2 hr.	Drainage	6.5307	0.0742	1.13	Lost	W. M.	50 Tailor	Neg.	48	++	++++ in 2 c.c. V 7	5555533100	Spinal parenchymatous. Tabetic syndrome	90
91	194	3/14/21	4	S.A.	0.2	2 hr.	Drainage	3.8499	0.0429	1.11	18.6	W. M.	50 Tailor	Neg.	27	+++	++++ in 2 c.c. V 8	5554444432	Spinal parenchymatous. Tabetic syndrome	91
92	134	2/ 4/21	32 2 S.A. 100 Hg	S.A.	0.2	2 hr.	Drainage	6.3795	0.0682	1.06	4.39	W. M.	41 Salesman	++++	16	Trace	++++ in 0.5 c.c. V Neg.	5555433110	Spinal parenchymatous. Tabetic syndrome	92
93	186	3/ 4/21	33 S.A.	S.A.	0.2	2 hr.	Drainage	4.2901	0.0466	1.08	12.8	W. M.	41 Salesman	++++	4	++	++++ in 0.5 c.c. V Neg.	5555544321	Spinal parenchymatous. Tabetic syndrome	93
94	332	4/15/21	34 S.A. 120 Hg	S.A.	0.2	2 hr.	Drainage	4.8871	0.0513	1.04	113.0	W. M.	41 Salesman	++++	21	++	++++ in 0.5 c.c. V Neg.	5555555442	Spinal parenchymatous. Tabetic syndrome	94
95	385	5/13/21	35 S.A. 125 Hg	S.A.	0.2	2 hr.	Drainage	6.4946	0.0700	1.07	3.57	W. M.	41 Salesman	++++	18	++	++++ in 0.5 c.c. V Neg.	2244232222	Spinal parenchymatous. Tabetic syndrome	95
96	471	6/17/21	36 S.A. 127 Hg	S.A.	0.2	2 hr.	Drainage	4.4065	0.0468	1.06	4.27	W. M.	41 Salesman	++++	15	++	++++ in 0.5 c.c. V Neg.	5555442110	Spinal parenchymatous. Tabetic syndrome	96
97	526	7/22/21	40 S.A. 129 Hg	S.A.	0.2	2 hr.	Drainage	7.0957	0.0774	1.09	6.4	W. M.	41 Salesman	++++	16	++	++++ in 0.5 c.c. V Neg.	5555544211	Spinal parenchymatous. Tabetic syndrome	97
98	182	3/ 7/21	14-8 Arsph. 6 S.A. 10 Hg	S.A.	0.2	2 hr.	Drainage	6.3371	0.0644	1.01	0	W. M.	48 Butcher	++++	3	Trace	+++ in 2 c.c. V 8	1233300000	Spinal parenchymatous. Tabetic syndrome	98
99	472	6/27/21	22 S.A. 10 Hg	S.A.	0.2	2 hr.	Drainage	4.1673	0.0417	1.00	2.4	W. M.	48 Butcher	++++	Neg.	+	Neg. in 2 c.c. V Neg.	1100000000	Spinal parenchymatous. Tabetic syndrome	99

TABLE I—Cont'd

100	497	7/ 6/21	14	S.A.	0.2	2 hr.	Drainage	4.0410	0.0465	1.15	0	W. M.	50 Butcher	Neg.	Neg.	Neg.	Neg. in 2 c.c. V 8	2222110000	Spinal parenchymatous. Tabetic syndrome	100
101	98	2/ 7/21	25 5 S.A. 30 Hg	S.A.	0.1	2 hr.	Drainage	5.6610	0.0529	0.93	13.2	W. M.	40 Rooming-House Keeper	++	Neg.	Neg.	+ in 2 c.c. V 3	0113200000	Spinal parenchymatous. Tabetic syndrome	101
102	193	3/14/21	28 30 Hg	S.A.	0.2	2 hr.	Drainage	4.8078	0.0510	1.06	9.8	W. M.	40 Rooming-House Keeper	Neg.	1	Trace	++++ in 2 c.c. V 7.5	2221110000	Spinal parenchymatous. Tabetic syndrome	102
103	288	4/ 6/21	29	S.A.	0.2	2 hr.	Drainage	5.5265	0.0560	1.01	4.4	W. M.	40 Rooming-House Keeper	Neg.	1	Neg.	+ in 2 c.c.	2222111000	Spinal parenchymatous. Tabetic syndrome	103
104	452	6/13/21	30	S.A.	0.2	2 hr.	Drainage	4.9614	0.0505	1.01	1.98	W. M.	40 Rooming-House Keeper	Neg.	1	+	+ in 2 c.c. V 4	1111000000	Spinal parenchymatous. Tabetic syndrome	104
105	177	3/ 4/21	25 1 S.A. 40 Hg	S.A.	0.2	2 hr.	Drainage	5.0977	0.0530	1.03	5.66	W. M.	51 Driver	+	2	Neg.	Neg. in 2 c.c. V 7.5	————	Spinal parenchymatous. Tabetic syndrome. Double optic atrophy, almost complete	105
106	433	6/ 8/21	26 42 Hg	S.A.	0.2	2 hr.	Drainage	4.3870	0.0455	1.03	2.2	W. M.	51 Driver	Neg.	1	Neg.	Neg. in 2 c.c. V 8	1111111000	Spinal parenchymatous. Tabetic syndrome. Double optic atrophy, almost complete	106
107	1922	7/ 5/22	2 S.A. 4 Hg	S.A.	0.2	2 hr.	Drainage	4.7275	0.0535	1.12	3.73	W. M.	58 Laborer	Neg.	1	Neg.	Neg. in 2 c.c.	0000000000	Spinal parenchymatous. Tabetic syndrome. Clinical arrest. Serologic cure	107
108	135	2/ 7/21	13-12 Arsph. 1 S.A. 15 Hg	S.A.	0.1	2 hr.	S.E. + 1/5	7.1687	0.0689	0.96	17.4	W. M.	36 Chauffeur	+++	5	+	++++ in 0.5 c.c. V Neg.	5544310000	Cerebrospinal parenchymatous Taboparetic syndrome	108
109	181	3/ 7/21	14	S.A.	0.2	2 hr.	S.E. + 1/5	5.2078	0.0537	1.03	14.8	W. M.	36 Chauffeur	+++	6	++	++++ in 1 c.c. V Neg.	2345433310	Cerebrospinal parenchymatous. Taboparetic syndrome	109
110	248	3/28/21	17	S.A.	0.2	2 hr.	S.E. + 1/5	6.6730	0.0681	1.02	33.0	W. M.	36 Chauffeur	+++	8	+	++++ in 0.5 c.c. V 6	5552321110	Cerebrospinal parenchymatous Taboparetic syndrome	110
111	165	2/25/21	31-3 S.A.	S.A.	0.2	2 hr.	Drainage	5.5181	0.0605	1.09	13.0	W. M.	37 Salesman, Dead	+	27	++	++++ in 2 c.c. V 3.5	5555555332	Cerebrospinal parenchymatous. Taboparetic syndrome	111
112	478	6/22/21	17 15 Hg	S.A.	0.1	2 hr.	Drainage	5.7260	0.0602	1.05	6.6	W. M.	37 Gambler	++++	5	+++	++++ in 0.5 c.c. V Neg.	5553211000	Cerebrospinal parenchymatous. Taboparetic syndrome	112
113	531	7/13/21	21	S.A.	0.2	2 hr.	Drainage	5.6579	0.0657	1.16	0.76	W. M.	37 Gambler		3	++	++++ in 0.5 c.c. V Neg.	5555444222	Cerebrospinal parenchymatous. Taboparetic syndrome	113
114	477	6/24/21	12-4 Arsph. 8 S.A. 15 Hg	S.A.	0.2	2 hr.	Drainage	5.9645	0.0637	1.06	Trace	W. M.	42 Mechanic	Neg.	Neg.	Neg.	Neg. in 2 c.c.	2221111100	Unconfirmed syphilis. Incomplete tabetic syndrome	114
115	479	6/20/21	5 21 Hg	S.A.	0.2	2 hr.	Drainage	4.3901	0.0523	1.19	1.9	W. F.	30 Housewife	+++	1	Neg.	Neg. in 2 c.c. V 6	2321100000	Latent syphilis. Hyperpituitarism. Anxiety psychoneurosis	115
116	294	4/ 1/21	1	S.A.	0.2	2 hr.	Drainage	7.2532	0.0724	0.998	55.3	W. F.	47 Housewife	++++ V 7.5	Neg.	Neg.	Neg. in 2 c.c. V 4.5	2222211100	Latent syphilis. Anxiety psychoneurosis. Wife of a tabetic patient	116
117	501	7/ 8/21	8	S.A.	0.2	1 hr.	Drainage	5.3673	0.0677	1.26	0.73	W. F.	42	Neg.	1	Trace	Neg. in 2 c.c. V 6	1110000000	Cured (?) syphilis. Depressive psychosis	117

NOTE: The chemical records of two examinations, No. 33 and No. 90 ,were lost. In error one record of the 24 Hour Group was included.

LEGEND:
Arsph. signifies Arsphenamine.
S.A. signifies Silver Arsphenamine
Hg. signifies Mercurial Injection.
S.E. signifies Swift-Ellis.
V. signifies Vernes Reaction.

Table II
Twenty-four Hour Group

	PATIENT SERIAL NO.	DATE OF LAST INJECTION	NO. PREVIOUS INJECTIONS	DRUG USED	DOSE	TIME AFTER INJECTION	METHOD TREATMENT	WT. OF SPECIMEN		PER CENT SOLIDS	AS IN MG. PER 100 GR. SPEC.	RACE SEX	AGE OCCUPATION	BLOOD W. R.	CELLS	GLOB.	WASSERMANN (VERNES)	COLLOIDAL GOLD	CLASSIFICATION	
								MOIST	DRY											
1	159	2/24/21	9-4 Arsph. 5 S.A. 2 Hg	S.A.	0.2	24 hr.	S.E.+ 1/5	5.3425	0.0735	1.37	16.0	W. M.	56 Janitor	++	5	+	++++ in 2 c.c. V 3	5555443210	Cerebral vascular with secondary parenchymatous changes. Hemiplegia	1
2	1949	7/10/22	14	S.A.	0.2	24 hr.	S.E.	3.9248	0.0504	1.29	0	W. M.	40 Salesman	Neg.	Neg.	Neg.	++++ in 1 c.c. V 8	3321100000	Cerebral meningovascular+	2
3	79	2/ 4/21	56 I.V. (55 Arsph. 1 S.A.) 22 Hg	Arsph. S.A.	0.2	26 hr.	S.E.	6.3626	0.0762	1.19	6.5	F. W.	54 None		8	Trace	Neg. in 2 c.c.	5554211000	Cerebral meningovascular. Chronic syphilitic basilar meningitis. Paresis of left III and VIII nerves	3
4	1920	7/ 6/22	3 20 Hg	S.A.	0.2	24 hr.	S.E.	2.9266	0.0313	1.06	3.19	W. M.	23 Waiter	+++	25	+	++++ in 1 c.c.	5432100000	Cerebral meningovascular with depression psychosis	4
5	494	6/30/21	16-2 Arsph. 14 S.A. 16 Hg	S.A.	0.1	24 hr.	S.E.	7.0643	0.0781	1.10	3.2	W. M.	40 Watchman	Alcohol +	3	Neg.	++ in 1 c.c. V Neg.	1110000000	Spinal meningovascular. Chronic hypertrophic syphilitic cervical meningitis	5
6	123	2/14/21	20 I.V. 15 Hg	S.A.	0.1	24 hr.	S.E.+ 1/10 S.	6.7118	0.0711	1.05	4.9	W. M.	40	++++	1	Neg.	Neg. in 2 c.c. V 7.5	2231000000	Cerebrospinal meningovascular	6
7	25	1/25/21	13-10 Arsph. 3 S.A. 16 Hg	S.A.	0.1	24 hr.	S.E.+ 1/5 S.S.	6.5413	0.0674	1.003	2.96	W. M.	42 City Fireman	++++	5	Trace	++++ in 1 c.c. V 5	4444331000	Cerebrospinal meningovascular	7
8	247	3/31/21	16 20 Hg	S.A.	0.2	24 hr.	S.E.	6.3921	0.0680	1.06	98.0	W. M.	42 City Fireman	++++	1	Neg.	++++ in 2 c.c. V Neg.	2244443221	Cerebrospinal meningovascular	8
9	481	6/23/21	25 20 Hg	S.A.	0.2	24 hr.	S.E.	8.4541	0.0948	1.12	Trace	W. M.	42 City Fireman	++++	3	Neg.	++++ in 2 c.c. V Neg.	5442221111	Cerebrospinal meningovascular	9
10	429	6/ 2/21	5	S.A.	0.2	24 hr.	S.E.	8.2858	0.0800	0.96	0	W. M.	30	++++	49	++	++++ in 0.5 c.c. V Neg.	1100000000	Cerebrospinal meningovascular	10
11	376	5/ 3/21	36-26 Arsph. 10 S.A. 20 Hg	S.A.	0.2	24 hr.	S.E.+ 1/10	4.7169	0.0469	0.99	1.0	W. F.	34 Housewife	++	3	Neg.	Neg. in 2 c.c. V 6	1110000000	Cerebrospinal meningovascular	11
12	448	6/ 9/21	5	S.A.	0.2	24 hr.	S.E.	5.7328	0.0581	1.01	3.4	W. M.	37 Acrobat	++++			++++ in 1 c.c. V Neg.		Cerebrospinal meningovascular	12
13	502	7/ 7/21	7	S.A.	0.2	24 hr.	S.E.	9.1059	0.1147	1.25	8.7	W. M.	37 Acrobat	++++	3	+	++ in 1 c.c. V Neg.	5544221111	Cerebrospinal meningovascular	13
14	527	7/21/21	8	S.A.	0.2	24 hr.	S.E.	5.9681	0.0664	1.11	1.51	W. M.	37 Acrobat	+++	3	+	++ in 1 c.c. C V Neg.	5544221110	Cerebrospinal meningovascular	14
15	1778	5/17/22	22	S.A.	0.2	24 hr.	S.E.	4.7515	0.0544	1.14	1.83	W. M.	37 Acrobat	+++	Neg.	Neg.	++ in 1 c.c. C Neg. in 2 c.c. A		Cerebrospinal meningovascular	15
16	468	6/14/21	4 10 Hg	S.A.	0.2	24 hr.	S.E.	7.7002	0.0883	1.14	3.4	C. F.	40 Dressmaker	++++	9	+	++++ in 0.5 c.c.	5555422211	Cerebrospinal meningovascular. Psychoneurosis	16
17	131	2/14/21	6-3 Arsph. 3 S.A. 10 Hg	S.A.	0.1	24 hr.	S.E.+ 1/10 S.S.	5.3582	0.0562	1.04	21.4	W. M.	43 Farmer	Neg.	5	Neg.	Neg. in 2 c.c. V 8	2331000000	Cerebrospinal meningovascular	17
18	249	3/29/21	10	S.A.	0.2	24 hr.	S.E.+ 1/10 S.S.	4.8396	0.0506	1.04	19.7	W. M.	43 Farmer	Neg.	1	Neg.	Neg. in 2 c.c. V 7	1110000000	Cerebrospinal meningovascular. Anxiety psychoneurosis	18
19	336	4/19/21	11	S.A.	0.2	24 hr.	S.E.+ 1/10 S.S.	5.2505	0.0560	1.06	Trace	W. M.	43 Farmer	Neg.	4	Neg.	Neg. in 2 c.c. V 7	1110000000	Cerebrospinal meningovascular. Anxiety psychoneurosis	19
20	189	2/21/21	5-3 Arsph. 2 S.A. 100 Hg	Arsph. S.A.	0.2	26 hr.	Drainage	4.3450	0.0525	1.20	6.2	C. M.	43 Waiter		70	+	++++ in 2 c.c. V ½	4544532100	Cerebrospinal meningovascular	20
21	2010	8/14/22	22 30 Hg	S.A.	0.2	24 hr.	S.E.	2.7396	0.0391	1.42	Trace	W. M	53 Clerk	++++	1	Trace	++++ in 2 c.c. V Neg. 8/17/21	0000232111	Cerebrospinal meningovascular	21
22	1685	4/19/22	26 21 Hg	S.A.	0.2	24 hr.	S.E.	3.5026	0.0362	1.03	30.3	W. M.	36 Shoemaker	++++	2	Neg.	++++ in 1 c.c.	1111100000	Cerebrospinal meningovascular. Psychoneurosis	22

TABLE II—Cont'd

23	1686	4/29/22	23 34 Hg	S.A.	0.2	24 hr.	S.E.	4.4087	0.0423	0.95	Trace	C. M.	48 Porter	+++	Neg.	Neg.	Neg. in 2 c.c.	1112110000	Cerebrospinal mixed. Bilateral optic atrophy, moderate degree	23
24	318	4/12/21	64	S.A.	0.2	24 hr.	S.E.+ 1/10	5.7413	0.0536	0.93	155.5	W. M.	45 Peddler	++++	1	Neg.	Neg. in 2 c.c.		Cerebrospinal mixed. Bilateral optic atrophy, extreme	24
25	345	4/21/21	5 3 Hg	S.A.	0.2	24 hr.	S.E.+ 1/10	6.3552	0.0797	1.25	3.4	C. F.	40 Clerk	++++	17	++	++++ in 0.5 c.c. V Neg.	5555555222	Cerebrospinal mixed. Paretic syndrome	25
26	1921	7/ 6/22	21 25 Hg	S.A.	0.2	24 hr.	S.E.	5.3134	0.0580	1.09	1.72	W. M.	29 Soldier	++++	8	++	++++ in 1 c.c.	5555544221	Cerebral parenchymatous. Paretic syndrome	26
27	1822	5/31/22	12 10 Hg	S.A.	0.2	24 hr.	S.E.	4.5100	0.0528	1.14	0	W. M.	39 Laborer	+	Neg.	Neg.	++ in 2 c.c.	3444321000	Cerebral parenchymatous. Paretic syndrome	27
28	334	4/14/21	8 15 Hg	S.A.	0.2	24 hr.	S.E.	4.4167	0.0462	1.04	Trace	W. F.	35 Housewife	++++	21	+	++++ in 0.5 c.c. V Neg.	5555544222	Spinal parenchymatous. Tabetic syndrome	28
29	378	5/ 3/21	4 15 Hg	S.A.	0.2	24 hr.	S.E.+ 1/10 S.S.	3.7299	0.0396	1.06	7.6	W. F.	35 Housewife	++++	5	Neg.	++ in 1 c.c. V 5	2221111000	Spinal parenchymatous. Tabetic syndrome	29
30	387	5/12/21	8-6 Arsph. 2 S.A. 16 Hg	S.A.	0.2	24 hr.	S.E.	5.4497	0.0578	1.06	0	W. M.	50 Musician	+	10	Trace	Neg. in 2 c.c. V 5	1111110000	Spinal parenchymatous. Tabetic syndrome.	30
31	375	5/ 4/21	15-5 Arsph. 10 S.A. 16 Hg	S.A.	0.2	24 hr.	Drainage	5.9151	0.0614	1.03	19.5	W. M.	41 Mechanic	++++	1	Neg.	++++ in 2 c.c. V 3.5	5555422111	Spinal parenchymatous. Tabetic syndrome	31
32	290	4/ 5/21	11-8 Arsph. 3 S.A. 17 Hg	S. A.	0.2	24 hr.	S.E.+ 1/10	7.1771	0.0739	1.02	5.4	W. F.	45 Housewife	++++			Neg. in 2 c.c. V 6		Spinal parenchymatous. Tabetic syndrome	32
33	585	7/28/21	2 8 Hg	S.A.	0.2	24 hr.	S.E.	5.2727	0.0539	1.02	9.27	C. M.	54 Waiter		2	Neg.	Neg. in 2 c.c. V 5	3332210000	Spinal parenchymatous. Tabetic syndrome	33
34	450	6/ 9/21	11	S.A.	0.2	24 hr.	S.E.	7.7928	0.0843	1.08	1.19	W. M.	52 Dockhand	+++	17	++	++++ in 0.5 c.c. V Neg.	4422111000	Spinal parenchymatous. Tabetic syndrome	34
35	394	5/19/21	14-9 Arsph. 5 S.A. 30 Hg	S.A.	0.2	24 hr.	S.E.	4.4102	0.0485	1.09	14.4	W. M.	50	Neg.	Neg.	Neg.	++ in 2 c.c. V 6	2222111100	Spinal parenchymatous. Tabetic syndrome+	35
36	500	6/30/21	31-21 Arsph. 10 S.A. 20 Hg	S.A.	0.2	24 hr.	S.E.	5.2745	0.0592	1.12	0.84	W. M.	40 Rooming-House Keeper	+++	Neg.	+	++++ in 0.5 c.c. V Neg.	2211000000	Spinal parenchymatous. Tabetic syndrome	36
37	1912	6/28/22	20	S.A.	0.2	24 hr.	S.E.	5.1487	0.0587	1.14	0.865	W. M.	47 Watchman	+++					Spinal parenchymatous. Tabetic syndrome	37
38	1821	5/31/22	19 16 Hg	S.A.	0.2	24 hr.	S.E.	3.3315	0.0363	1.09	2.75	W. M.	47 Watchman	+++	4	Trace	+ in 2 c.c.	2223321000	Spinal parenchymatous. Tabetic syndrome	38
39	1788	5/25/22	22 S.A. 36 Hg	S.A.	0.2	24 hr.		4.6112	0.0566	1.22	10.6	W. M.	41 Engineer	Neg.	9				Spinal parenchymatous. Tabetic syndrome	39
40	1454	3/10/22	12 S.A. 25 Hg	S.A.	0.2	24 hr.		4.1212	0.0445	1.07	Trace	W. M.	41 Engineer	+	10	+	++++ in 1 c.c.		Spinal parenchymatous. Tabetic syndrome	40
41	1909	6/29/22	16-12 Arsph. 4 S.A. 21 Hg	S.A.	0.2	24 hr.	S.E. + 1/10 S.S.	5.2045	0.0603	1.15	66.3	W. M.	41 Salesman	+	23	++	++++ in 2 c.c.		Spinal parenchymatous. Tabetic syndrome	41
42	1860	6/13/22	12 Arsph. 21 Hg	S.A.	0.2	24 hr.	S.E.	3.8835	0.0564	1.45	5.31	W. M.	41 Salesman	+	25	Trace	+++ in 1 c.c.	2333210000	Spinal parenchymatous. Early tabetic syndrome	42
43	2092	9/12/22	21-12 Arsph. 7 S.A. 2 Neos 21 Hg	S.A.	0.2	24 hr.	S.E.					W. M.	41 Salesman	+	Neg.	Neg.	+++ in 1 c.c.	0000000000	Spinal parenchymatous. Early tabetic syndrome	43
44	324	4/14/21	18-12 Arsph. 6 S.A. 16 Hg	S.A.	0.2	24 hr.	S.E.	7.2880	0.0800	1.09	9.3	W. M.	36 Chauffeur	++++	4	Trace	++++ in 0.5 c.c. V 6	5555555544	Cerebrospinal parenchymatous. Taboparetic syndrome	44
45	160	2/24/21	11-10 Arsph. 1 S.A. 10 Hg	S.A.	0.2	24 hr.	S.E. + 1/5 S.S.	5.0080	0.1648	3.29	8.5	W. M.	31 Salesman	++++	12	+	++++ in 1 c.c. V 5	4554433210	Cerebrospinal parenchymatous. Taboparetic syndrome	45
46	321	4/12/21	2 12 Hg	S.A.	0.2	24 hr.	S.E. + 1/10	5.0903	0.0485	0.95	17.0	C. M.	28 Laborer	++++	1	Neg.	Neg. in 2 c.c.	1122211100	Peripheral. Right facial neuritis	46

NOTE: The chemical record in one case, No. 43, was lost.

Table III

Forty-eight Hour Group

	PATIENT SERIAL NO.	DATE OF LAST INJECTION	NO. PREVIOUS INJECTIONS	DRUG USED	DOSE	TIME AFTER INJECTION	METHOD TREATMENT	WT. OF SPECIMEN		PER CENT SOLIDS	AS IN MG. PER 100 GR. SPEC.	RACE SEX	AGE OCCUPATION	BLOOD W. R.	CELLS	GLOB.	WASSERMANN (VERNES)	COLLOIDAL GOLD	CLASSIFICATION	
								MOIST	DRY											
1	1718	4/24/22	11 14 Hg	S.A.	0.2	48 hr.	S.E.	3.3616	0.0322	0.95	15.5	W. M.	33 Salesman	++++	7	Trace	++++ in 2 c.c.	4333321000	Cerebral meningeal. Acute cerebral meningitis of the convexity	1
2	373	5/ 6/21	16-5 Arsph. 11 S.A. 16 Hg	S.A.	0.2	48 hr.	S.E. + 1/10 S.S.	5.6055	0.0591	1.05	Trace	W. M.	23 Auto Mechanic	Neg.	25	+	++++ in 2 c.c. V 3	4522211111	Cerebral meningeal. Subacute cerebral meningitis of the convexity	2
3	470	6/15/21	19 16 Hg	S.A.	0.2	48 hr.	S.E. + 1/10 S.S.	4.5779	0.0480	1.04	1.0	W. M.	23 Auto Mechanic	+	7	+	+++ in 1 c.c. V 7	4442211000	Cerebral meningeal. Subacute cerebral meningitis of the convexity	3
4	1746	5/ 3/22	20 10 Hg	S.A.	0.2	48 hr.	S.E.	3.0946	0.0299	0.96	3.34	C. F.	43 Housewife	Neg.	15	Trace	Neg. in 2 c.c.	3334421000	Cerebral meningovascular. Bilateral optic atrophy	4
5	1819	5/31/22	23 10 Hg	S.A.	0.2	48 hr.	S.E.	4.2173	0.0462	1.09	11.9	C. F.	43 Housewife	+ (?)	6	Neg.	Neg. in 2 c.c.	5554332100	Cerebral meningovascular. Bilateral optic atrophy	5
6	1779	5/17/22	16 S.A. 15 Hg	S.A.	0.2	48 hr.	S.E.	4.7215	0.0545	1.15	0	W. M.	56 Barber	++++	4	+	Neg. in 2 c.c.	2111000000	Cerebral mixed. Cerebral endarteritis with accompanying psychosis	6
7	1870	6/14/22	17	S.A.	0.2	48 hr.	S.E.	6.6986	0.0783	1.16	9.57	W. M.	56 Barber	+++	1	+	+++ in 2 c.c.	4433210000	Cerebral mixed. Cerebral endarteritis with accompanying psychosis	7
8	320	4/13/21	10-2 Arsph. 8 S.A. 16 Hg	S.A.	0.2	48 hr.	S.E. + 1/10 S.S.	4.7502	0.0500	1.05	1.00	W. M.	40 Watchman	++++	Neg.	Neg.	++++ in 2 c.c. V 5	————	Spinal meningovascular. Chronic syphilitic hypertrophic cervical meningitis	8
9	1913	6/28/22	16 16 Hg	S.A.	0.2	48 hr.	S.E.	5.0821	0.0524	1.03	Trace	W. M.	33 Store-Keeper	++++	1	+	++++ in 2 c.c.	5555554300	Cerebral meningovascular. Right hemiparesis	9
10	1983	8/ 7/22	24	S.A.	0.2	48 hr.	S.E.	2.6630	0.0284	1.06	3.52	W. M.	33 Store-Keeper	++	1	++	+++ in 1 c.c.	5555543210	Cerebral meningovascular. Right hemiparesis	10
11	1914	6/26/22	35 S.A.	S.A.	0.2	48 hr.	S.E.	5.0909	0.0398	0.78	10.50	W. M.	42 Fireman	++++	3	Neg.	++++ in 2 c.c. V 0	5442221110	Cerebrospinal meningovascular	11
12	319	4/13/21	18-11 Arsph. 7 S.A. 25 Hg	S.A.	0.2	48 hr.	S.E. + 1/10 S.S.	5.5877	0.0527	0.94	2.08	W. M.	42 Fireman	++++	1	Neg.	++++ in 0.2 c.c. V 0	2244443221	Cerebrospinal meningovascular	12
13	413	5/25/21	19 S.A. 28 Hg	S.A.	0.2	48 hr.	S.E.	5.0516	0.0501	0.99	4.99	W. M.	42 Fireman	++++	3	Neg.	++++ in 0.5 c.c. V 0	————	Cerebrospinal meningovascular	13
14	1968	7/12/22	21 20 Hg	S.A.	0.2	48 hr.	S.E.	3.9270	0.0407	1.03	24.5	W. M.	53 Clerk	++++	1	Trace	++++ in 2 c.c.	2211000000	Cerebrospinal meningovascular	14
15	2091	9/13/22	22	S.A.	0.2	48 hr.	S.E.					W. M.	53 Clerk	++++	1	Trace	++++ in 2 c.c.	0000231111	Cerebrospinal meningovascular	15
16	1681	4/19/22	16 25 Hg	S.A.	0.2	48 hr.	Drainage	4.9220	0.0505	1.02	26.4	W. M.	53 Clerk	++++	1	+	++++ in 0.5 c.c.	5555500000	Cerebrospinal meningovascular	16
17	1807	5/29/22	28 28 Hg	S.A.	0.2	48 hr.	S.E.	2.9343	0.0432	1.46	0	W. M.	36 Shoemaker	++++	15	+	++ in 1 c.c.	0000000000 (bloody)	Cerebrospinal meningovascular. Psychoneurosis	17
18	1902	6/19/22	29	S.A.	0.2	48 hr.	S.E.	5.2472	0.0612	1.14	0.817	W. M.	36 Shoemaker	Neg.	1	Trace	++++ in 1 c.c.	1000000000	Cerebrospinal meningovascular. Psychoneurosis	18
19	1950	7/10/22	33	S.A.	0.2	48 hr.	S.E.	4.0902	0.0653	1.35	0	W. M.	36 Shoemaker	Neg.	3	++	++++ in 0.5 c.c.	1100000000	Cerebrospinal meningovascular. Psychoneurosis	19
20	292	4/ 6/21	31 32 Hg	S.A.	0.2	48 hr.	S.E. + 1/10 S.S.	4.9990	0.0505	1.01	6.90	W. M.	38 Salesman	Neg.	Neg.	Neg.	Neg. in 2 c.c.	5555544333	Cerebrospinal meningovascular	20
21	1780	5/17/22	33 S.A. 14 Arsph 32 Hg	S.A.	0.2	48 hr.	S.E.	5.2510	0.0580	1.10	0.862	W. M.	42 Packer	Neg.	1	Neg.	Neg. in 2 c.c.	2333332100	Cerebrospinal meningovascular	21
22	1752	5/ 8/22	17 7 Hg	S.A.	0.2	48 hr.	S.E.	4.2005	0.0420	0.99	28.5	C. F.	40 Dressmaker	++++	Neg.	Trace	Neg. in 2 .0 c.c. C ++ in 2 c.c. A	5434321000	Cerebrospinal meningovascular. Psychoneurosis	22

TABLE III—Cont'd

23	482	6/22/21	66-6 S.A. 200 Hg	S.A.	0.2	48 hr.	S.E.	4.9378	0.0515	1.04	10.7	W. M	45 Peddler	++++	Neg.	Neg.	Neg. in 2 c.c. V 5	2221100000	Cerebrospinal mixed. Bilateral optic atrophy extreme	23
24	1808	5/29/22	14-9 Arsph. 5 S.A. 16 Hg	S.A.	0.2	48 hr.	S.E.	3.1450	0.0476	1.51	11.5	W. M.	42 Painter	++++	1	+	++ in 2 c.c.	5334432100	Cerebrospinal mixed. Bilateral optic atrophy with extreme exophthalmos	24
25	1818	5/31/22	35-8 S.A. 27 Arsph.	S.A.	0.2	48 hr.	L.P. only	1.1693	0.0098	0.830	0	W. F.	35 Housewife	Neg.	4	Neg.	Neg. in 2 c.c.	2334321000	Cerebrospinal mixed. Amyotrophy	25
26	1616	4/17/22	21 S.A.	S.A.	0.2	48 hr.	S.E. + 1/5 S.S.	5.1575	0.0560	1.08	3.57	W. M.	35 Salesman	+++	4	+	++++ in 2 c.c.	2222210000	Cerebral parenchymatous. Paretic syndrome	26
27	1790	5/24/22	9 15 Hg	S.A.	0.2	48 hr.	S.E.	5.6480	0.0680	1.20	0	W. M.	50 Clerk	++++	7	++	++++ in 0.5 c.c.	5555532000	Cerebral parenchymatous. Paretic syndrome	27
28	1751	5/ 8/22	11 10 Hg	S.A.	0.2	48 hr.	S.E.	2.6333	0.0268	1.01	74.6	W. M.	39 Laborer	+	3	Neg.	Neg. in 2 c.c.	2344321000	Cerebral parenchymatous. (G.P) Paretic syndrome (?)	28
29	1911	6/28/22	14	S.A.	0.2	48 hr.	S.E.	5.1738	0.0506	0.97	0	W. M.	39 Laborer	+ in A	0	Neg.	++ in 2 c.c.	3444321000	Cerebral parenchymatous. (G.P) Paretic syndrome (?)	29
30	297	4/ 6/21	6-5 Arsph. 1 S.A. 17 Hg	S.A.	0.2	48 hr.	S.E. + 1/10 S.S.	3.8529	0.0409	1.03	9.75	W. M.	60 Upholsterer	+++	Neg.	Neg.	+ in 2 c.c. A Neg. in 2 c.c. C	5554443322	Spinal parenchymatous. Tabetic syndrome	30
31	1785	5/22/22	11 Arsph. 1 S.A. 52 Hg	S.A.	0.2	48 hr.	S.E.	4.3563	0.0497	1.14	0	W. M.	37 Operator	Neg.	Neg.	Neg.	Neg. in 2 c.c.	1122100000	Spinal parenchymatous. Tabetic syndrome	31
32	1728	4/26/22	18 15 Hg	S.A.	0.2	48 hr.	S.E.	5.0909	0.0497	0.97	0	W. M	47 Watchman	++ in A	4	+	+ in 2 c.c.	2223321000	Spinal parenchymatous. Tabetic syndrome (6/21)	32
33	1871	6/14/22	17 15 Hg	S.A.	0.2	48 hr.	S.E.	5.4661	0.0519	0.94	1.60	W. M.	47 Actor	Neg.	Neg.	Trace	++ in 1 c.c.	3333210000	Spinal parenchymatous. Tabetic syndrome	33
34	1924	7/ 5/22	18	S.A.	0.2	48 hr.	S.E.	3.3350	0.0387	1.16	10.30	W. M.	47 Actor	Neg.	2	Trace	AC in 2 c.c.	———	Spinal parenchymatous. Tabetic syndrome	34
35	1923	7/ 5/22	7 8 Hg	S.A.	0.2	48 hr.	S.E.	4.3133	0.0493	1.14	Trace	W. M.	45 Chef	Neg.	0	Neg.	+++ in 0.5 c.c.	3221110000	Spinal parenchymatous. Tabetic syndrome	35
36	1747	5/ 3/22	58-12 S.A. 46 Arsph. 150 Hg	S.A.	0.2	48 hr.	S.E.	4.1929	0.0557	1.32	0	W. M.	41 Salesman	++++	12	+	++++ in 0.5 c.c.	5555554321	Spinal parenchymatous. Tabetic syndrome	36
37	1820	5/31/22	61-15 S.A. 46 Arsph. 155 Hg	S.A.	0.2	48 hr.	S.E.	4.4038	0.0559	1.27	Trace	W. M.	41 Salesman	++++	14	++	++++ in 0.5 c.c.	5555555432	Spinal parenchymatous. Tabetic syndrome	37
38	1910	6/28/22	66-17 S.A. 46 Arsph. 155 Hg	S.A.	0.2	48 hr.	S.E.	5.0676	0.0633	1.24	3.94	W. M.	41 Salesman	—	—	—	—	—	Spinal parenchymatous. Tabetic syndrome	38
39	95	2/ 7/21	22-21 Arsph. 1 S.A. 5 Hg	S.A.	0.1	48 hr.	S.E. + 1/10	5.4964	0.0608	1.10	32.0	W. M.	36 Auto Supplies	Neg.	1	Neg.	Neg. in 2 c.c. V 6.5	1223332100	Spinal parenchymatous. Tabetic syndrome	39
40	38	1/28/21	6-5 Arsph. 1 S.A. 15 Hg	S.A.	0.1	48 hr.	S.E. + 1/10 S.S.	7.0415	0.0794	1.11	4.4	W. F.	47 Housewife	++++	Neg.	Neg.	Neg. in 2 c.c.	2222100000	Spinal parenchymatous. Tabetic syndrome	40
41	144	3/ 2/21	7	S.A.	0.1	48 hr.	S.E. + 1/10 S.S.	5.2180	0.0548	1.05	4.5	W. F.	47 Housewife	+++	2	Trace	Neg. in 2 c.c. V 7	5443321000	Spinal parenchymatous. Tabetic syndrome	41
42	286	4/ 8/21	8 S.A. 15 Hg	S.A.	0.2	48 hr.	S.E. + 1/10 S.S.	7.0045	0.0715	1.02	3.5	W. F.	47 Housewife	+++	Neg.	Neg.	Neg. in 2 c.c. V 2	4444422222	Spinal parenchymatous. Tabetic syndrome	42
43	374	5/ 6/21	17-6 Arsph. 11 S.A. 17 Hg	S.A.	0.2	48 hr.	S.E.	6.4946	0.0681	1.04	1.4	W. F.	29 Housewife	++++	3	Trace	+++ in 2 c.c. V 5.5	2222110000	Spinal parenchymatous. Tabetic syndrome. Right optic atrophy	43
44	246	3/30/21	10-1 S.A. 9 Arsph.	S.A.	0.2	48 hr.	S.E. + 1/5 S.S.	4.4694	0.0468	1.05	16.03	W. M.	50	Neg.	1	Trace	Neg. in 2 c.c. V 7	2222311000	Spinal parenchymatous. Tabetic syndrome	44
45	43	1/28/21	14-12 Arsph. 2 S.A.	S.A.	0.1	48 hr.	Drainage	5.9906	0.0711	1.18	5.6	W. M.	37 Salesman, Dead	Neg.	17	++	++++ in 2 c.c. V 1.5	5555544310	Cerebrospinal parenchymatous. Taboparetic syndrome	45
46	1846	6/ 5/22	11 18 Hg	S.A.	0.2	48 hr.	S.E.	5.3050	0.0589	1.11	0	W. M.	50	Neg.	Neg.	Neg.	Neg. in 2 c.c.	2222110000	Spinal parenchymatous. Tabetic syndrome	46
47	252	3/23/21	12-10 Arsph. 2 S.A. 10 Hg	S.A.	0.2	48 hr.	S.E. + 1/5 S.S.	5.9376	0.0622	1.05	19.3	W. M.	31 Salesman	++++	4	+	++++ in 1 c.c. V 4	2222111100	Cerebrospinal parenchymatous. Taboparetic syndrome	47

NOTE: The chemical record in one case, No. 15, was lost.

Table IV

Seventy-two Hour Group

	Patient Serial No.	Date of Last Injection	No. Previous Injections	Drug Used	Dose	Time after Injection	Method Treatment	Wt. of Specimen		Per Cent Solids	As in Mg. per 100 Gr. Spec.	Race Sex	Age Occupation	Blood W. R.	Cells	Glob.	Wassermann (Vernes)	Colloidal Gold	Classification	
								Moist	Dry											
1	351	4/25/21	8 10 Hg	S.A.	0.2	72 hr.	S.E. + 1/10 S.S.	5.1317	0.0520	0.99	4.8	W. M.	26 Chauffeur	Neg.	17	Trace	Neg. in 2 c.c. V 7.5	4422111000	Cerebral meningeal. Acute syphilitic cerebral meningitis of the convexity with anxiety, psychoneurosis	1
2	393	5/18/21	9 10 Hg	S.A.	0.2	72 hr.	S.E.	4.7422	0.0468	0.98	192.0	W. M.	26 Chauffeur	Neg.	29	+	Neg. in 2 c.c. V 7.5	4442221111	Cerebral meningeal. Acute syphilitic cerebral meningitis of the convexity with anxiety, psychoneurosis	2
3	436	6/ 6/21	10 10 Hg	S.A.	0.2	72 hr.	S.E.	7.0100	0.0709	1.01	4.2	W. M.	26 Chauffeur	Neg.	1	Neg.	Neg. in 2 c.c. V 7	2221111000	Cerebral meningeal. Acute syphilitic cerebral meningitis of the convexity with anxiety, psychoneurosis	3
4	1743	5/ 1/22	12 10 Hg	S.A.	0.2	72 hr.	Drainage	3.1462	0.0356	1.13	0	W. M.	37 Salesman	Neg.	0	Trace	Neg. in 2 c.c. V 6 (8/3/21)	5555543210	Cerebral meningovascular. Anxiety, psychoneurosis	4
5	1744	5/ 1/22	23-1 Arsph. 22 S.A. 30 Hg	S.A.	0.2	72 hr.	S.E.	2.8871	0.0287	0.99	1.74	W. M.	56 Jeweler	++++	1	Trace	Neg. in 2 c.c.	2222231000	Cerebral meningovascular	5
6	1745	5/ 5/22	11 20 Hg	S.A.	0.2	72 hr.	S.E.	6.4058	0.0634	0.99	4.73	W. M.	33 Store-Keeper	++++	1	+	++ in 1 c.c.	5555554300	Cerebral meningovascular. Right hemiparesis	6
7	352	4/25/21	10 Arsph. 10 S.A. 5 Hg	S.A.	0.2	72 hr.	S.E. + 1/10	5.8700	0.0607	1.03	Trace	W. M.	38 Driver	Neg.	0	Neg.	Neg. in 2 c.c.	1221110000	Cerebral meningovascular. Hysteria	7
8	1682	4/19/22	19 12 Hg	S.A.	0.2	72 hr.	S.E.	4.3908	0.0441	1.004	0	C. F.	43 Housewife	+ (?)	5	Trace	+++ in 2 c.c.	1112221000	Cerebral meningovascular	8
9	258	4/ 4/21	24-3 S.A. 21 Arsph. 17 Hg	S.A.	0.2	72 hr.	S.E. + 1/10	5.7498	0.0633	1.10	31.6	W. M.	60 Retired	++++	5	Neg.	++++ in 2 c.c.	1111000000	Cerebral meningovascular Chronic syphilitic basilar meningitis with ophthalmoplegia	9
10	1967	7/14/22	17 17 Hg	S.A.	0.2	72 hr.	S.E.	6.2186	0.0679	1.09	2.94	W. M.	56 Barber	+++	+	+	++++ in 0.1 c.c.	1111100000	Cerebral vasculoparenchymatous. Cerebral endarteritis with accompanying psychosis	10
11	392	5/16/21	11 16 Hg	S.A.	0.2	72 hr.	S.E. + 1/10	3.2200	0.03110	0.96	19.3	W. M.	40 Watchman	++++	1	Trace	++++ in 2 c.c. V 4	2221111100	Spinal meningovascular. Chronic hypertrophic cervical meningitis. Amyotrophy	11
12	524	7/18/21	17 17 Hg	S.A.	0.1	72 hr.	S.E.	5.6945	0.0577	1.01	3.0	W. M.	40 Watchman	++++	5	Neg.	++++ in 0.5 c.c. V Neg.	4444332211	Spinal meningovascular. Chronic hypertrophic cervical meningitis. Amyotrophy	12
13	435	6/ 6/21	20-10 Arsph. 10 S.A. 30 Hg	S.A.	0.2	72 hr.	S.E.	3.9968	0.0408	1.02	Trace	W. M.	42 Fireman	++++	5	Neg.	++++ in 0.5 c.c. V Neg.	4422211000	Cerebrospinal meningovascular	13
14	1903	6/23/22	9 1 Hg	S.A.	0.2	72 hr.	S.E. + 1/5	5.2293	0.0565	1.08	0.884	W. M.	60 Laborer	++++	12	++	++++ in 1 c.c.	4322100000	Cerebrospinal meningovascular	14
15	1770	5/12/22	28	S.A.	0.2	72 hr.	S.E.	3.9709	0.0326	0.82	0	W. M.	36 Shoemaker	++++	5	Neg.	+ in 0.5 c.c.	3332110000	Cerebrospinal meningovascular. Anxiety psychoneurosis	15
16	530	7/15/21	5 6 Hg	S.A.	0.2	72 hr.	S.E.	3.9140	0.0436	1.11	0	C. F.	40 Dressmaker	++++	3	Neg.	++++ in 2 c.c. V Neg.	5554221100	Cerebrospinal meningovascular. Psychoneurosis	16

TABLE IV—Cont'd

17	396	5/18/21	13 17 Hg	S.A.	0.2	72 hr.	S.E. + 1/10	5.7271	0.0657	1.14	73.0	W. M.	42 Peddler	++++	1	Neg.	+++ in 1 c.c. V 4	4444322111	Cerebrospinal mixed. Bilateral optic atrophy with extreme exophthalmos	17
18	523	7/20/21	14	S.A.	0.2	72 hr.	S.E.	6.8306	0.0742	1.08	3.3	W. M.	42 Peddler	++++	3	Neg.	Neg. in 2 c.c. V 8	2222211111	Cerebrospinal mixed. Bilateral optic atrophy with extreme exophthalmos	18
19	296	4/ 7/21	3 3 Hg	S.A.	0.2	72 hr.	S.E. + 1/10	7.4610	0.0845	1.13	16.5	W. M.	35 Clerk	++++	2	++	++++ in 0.5 c.c. V Neg.	5555555222	Cerebral parenchymatous. Paretic syndrome	19
20	386	5/13/21	13 15 Hg	S.A.	0.2	72 hr.	S.E.	5.3060	0.0528	0.99	0	W. F.	47 Housewife	++++	1	Neg.	++ in 2 c.c. V 5.5	1110000000	Spinal parenchymatous. Tabetic syndrome	20
21	532	7/13/21	1 5 Hg	S.A.	0.2	72 hr.	S.E.	5.0260	0.0559	1.11	5.3	C. M.	54 Waiter		2	Neg.	Neg. in 2 c.c. V 5	3332210000	Spinal parenchymatous. Tabetic syndrome	21
22	353	4/25/21	5	S.A.	0.2	72 hr.	S.E. + 1/10	4.3420	0.0468	1.07	3.28	W. M.	52 Dockhand	+++	19	++	+++ in 0.5 c.c. V Neg.	5555542200	Spinal parenchymatous. Tabetic syndrome.	22
23	389	5/16/21	8	S.A.	0.2	72 hr.	S.E. + 1/10	5.6804	0.0619	1.08	0.808	W. M.	52 Dockhand	+++	21	++	++++ in 0.5 c.c. V Neg.	5555554222	Spinal parenchymatous. Tabetic syndrome	23
24	473	6/27/21	13	S.A.	0.2	72 hr.	S.E.	3.0704	0.0336	1.09	1.49	W. M.	52 Dockhand	+++	1	++	++++ in 0.5 c.c.	———	Spinal parenchymatous. Tabetic syndrome	24
25	496	6/29/21	20-10 S.A. 10 Arsph. 7 Hg	S.A.	0.1	72 hr.	S.E.	5.6348	0.0619	1.09	8.08	W. M.	38 Watchman	+++	19	+	++++ in 0.5 c.c. V Neg.	2221111000	Spinal parenchymatous. Tabetic syndrome	25
26	449	6/13/21	15-4 S.A. 9 Arsph.	S.A.	0.2	72 hr.	S.E.	5.9128	0.0622	1.05	0.804	W. M.	50	Neg.	0	Neg.	Neg. in 2 c.c. V 6 (5/19/21)	1111100000	Spinal parenchymatous. Tabetic syndrome	26
27	1683	4/17/22	25	S.A.	0.2	72 hr.	S.E. + 1/5 S.S.	2.1906	0.0210	0.95	1.13	W. M.	41 Mechanic	+	0	Neg.	Neg. in 2 c.c.	5544321000	Spinal parenchymatous. Tabetic syndrome	27
28	1456	3/17/22	30 Hg 21-5 Arsph. 16 S.A.	S.A.	0.2	72 hr.	S.E. + 1/5	4.7904	0.0438	0.91	9.13	W. M.	41 Mechanic	+	1	+	++++ in 2 c.c.	5555432100	Spinal parenchymatous. Tabetic syndrome	28
29	1817	6/ 2/22	27	S.A.	0.2	72 hr.	S.E.	4.4437	0.0543	1.22	1.84	W. M.	41 Mechanic	+	4	+	++++ in 2 c.c.	5555555432	Spinal parenchymatous. Tabetic syndrome	29
30	1734	4/29/22	5 15 Hg	S.A.	0.2	72 hr.	S.E.	3.5909	0.0349	0.94	11.40	W. M.	36 Barber	++	1	Trace	Neg. in 2 c.c.	3333210000	Spinal parenchymatous. Tabetic syndrome	30
31	1769	5/12/22	36 5 S.A. 50 Hg	S.A.	0.2	72 hr.	S.E.	3.2103	0.0341	1.06	2.92	W. M.	40 Tailor	Neg.	0	Neg.	Neg. in 2 c.c.	1111100000	Spinal parenchymatous. Tabetic syndrome. Completely arrested	31
32	1966	7/14/22	14 1 Hg	S.A.	0.2	72 hr.	Drainage	2.5875	0.0272	1.05	3.67	W. M.	46 Tailor	+++	4	Neg.	+++ in 0.5 c.c.	1111100000	Spinal parenchymatous. Tabetic syndrome	32
33	1853	6/ 9/22	7 6 Hg	S.A.	0.2	72 hr.	S.E.	3.4233	0.0241	0.70	0	W. M.	45 Chef	+++					Spinal parenchymatous. Tabetic syndrome	33

SULFARSENOL IN THE TREATMENT OF SYPHILIS

A Preliminary Report*

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NONE of us will doubt for a moment that the physician has a most effective weapon in the arsenical preparations, arsphenamine and neoarsphenamine, to combat the ravages of the syphilitic virus. Since Ehrlich's discovery various other arsenical preparations have been used with more or less success. One of the most recent of these to be placed before the American profession is sulfarsenol, a French preparation supposedly hailed with "great success" in Europe.

Sulfarsenol, according to the manufacturers, is a sulphur arsphenamine product with a formula $C_{14}H_{14}O_8S_2As_2N_2Na$. It is a fine yellow powder, possessing an odor strongly suggesting a sulphide, readily soluble in water and capable of being exposed to air for hours without decomposing.

At the request of Dr. Howard Fox, who had received a small supply of the product for purposes of experimentation, sulfarsenol was employed in the Out-Patient Department of Harlem Hospital in treating cases of active syphilis with cutaneous lesions. The patients were chosen at random as they applied for treatment. As our clinic did not have the aid of a social service worker it was found most difficult to induce the patients to return at desired intervals. Thus it will be seen that out of 41 cases only 20 were followed to complete disappearance of the lesions, or until conclusions of some value could be made.

Technic.—Asepsis was fully observed at all times. The neck of the ampoule was broken, then filled with distilled water and after complete solution, the fluid was drawn into the syringe and injected after proper dilution was made. For intravenous use the amount given was diluted in 20 c.c. of water, in 2 c.c. for subcutaneous injections, while for the intramuscular route the dilution varied from 2 to 5 c.c. For this latter method of administration the same procedure was employed as in giving injections of insoluble mercurial preparations. The lateral aspect of the arm was the site chosen for subcutaneous injection. Treatments were given at 4 to 5 day intervals. The average dose injected by all methods was gram 0.36, comparatively small when compared with gram 0.9, the maximum neoarsphenamine dose.

Use of the Drug Intravenously.—Sulfarsenol affected favorably all types of syphilitic skin lesions treated. It appeared to be most effective in causing the disappearance of the annular syphilide (a secondary manifestation frequently seen in negroes). At the other extreme the papulopustular lesions were the most resistant to this form of medication. From the appended chart it will be seen that 2 to 3 doses were required to considerably improve the skin lesions, while 5 to 6 were required to cause their complete involution. This is to be judged a fairly good therapeutic result, if the amount of each injected dose of the drug is to be taken into consideration. As regards the immediate or remote by-effects, nothing of a serious nature was observed or disclosed by the patients on questioning, beyond the fact that upon two separate occasions numbness and paraesthesia, limited chiefly to both extremities, were noted. This was not very annoying in character, appearing a few hours after treatment and continuing to persist the following day.

Use of the Drug Intramuscularly.—The lesions were favorably affected to the same extent in all cases, their disappearance being quite as rapid as when the intravenous route was used. In one case the injection of 0.3 gram caused marked improvement of an annular syphilide, this observation being recorded four days after injection. As might be expected, this method of treatment has some disadvantages, all of which are local. Of the 6 cases under observation, 5 complained bitterly of pain which appeared soon after injection and became more intense on the following day. It was still present four days later when the patients appeared for observation. The majority were unable to walk or sit down without suffering marked pain. The sixth individual who had remarked that the pain was very slight discontinued treatment before the skin lesions had completely disappeared. Local tenderness at the site of previous injections was present in all cases. At no time were there any objective signs

TABLE I

INTRAMUSCULAR INJECTIONS OF SULFARSENOL

NO.	SEX	AGE	TYPE OF ERUPTION	NUMBER INJECT.	TOTAL AMOUNT IN GRAMS	DURATION OF TREAT.	CLIN. RESULTS	WASS. BEFORE	WASS. AFTER
1	M	30	II Papular (recurrent)	4	1.74	14 days	Complete disappearance skin lesions	4 plus	2 plus
2	M	22	II Maculopustular	4	1.68	17 days	Complete disappearance skin lesions	1 plus	1 plus
3	F	56	III Nodular (ulcerative)	3	1.08	16 days	Lesions markedly improved	4 plus	not taken
4	M	37	I-II Genital chancre. Annular.	1	.30	4 days	Marked improvement of annular lesion after one inject. Discontinued treatment.	4 plus	not taken
5	F	32	III Nodular (right leg and right forearm)	4	1.14	17 days	Lesions on forearm disappeared completely. Slight evidence of disease on leg. Discontinued treatment.	3 plus	not taken
6	M	24	III Ulcerating gumma (tonsil)	2	.78	4 days	Lesions clearing. Evidences of healing. Discontinued treatment.	4 plus	not taken

I – primary }
II– secondary } stage
III–tertiary }

of infiltration nor were there any general symptoms complained of or observed.

Use of the Drug Subcutaneously.—Experience with the subcutaneous administration of sulfarsenol was very limited, four patients being treated with a total of eleven injections. Of these patients, 3 failed to continue treatment while one is still under observation. As far as can be judged by this limited experience, the lesions disappeared as quickly after subcutaneous as after intravenous injections. When small doses were given (gram 0.6 – .18) there was

TABLE II

INTRAVENOUS INJECTIONS OF SULFARSENOL

NO.	SEX	AGE	TYPE OF ERUPTION	NUMBER INJECT.	TOTAL AMOUNT IN GRAMS	DURATION OF TREAT.	CLIN. RESULTS	WASS. BEFORE	WASS. AFTER
1	F	24	II Annular mucous patches	3	.72	23 days	Lesions disappeared after 3rd treatment.	4 plus	not taken
2	F	20	II Papulo-pustular	7	2.25	44 days	Lesions disappeared after 7th treatment.	4 plus	1 plus
3	M	52	II Pustular	7	1.94	33 days	Lesions disappeared after 7th treatment.	4 plus	not taken
4	M	33	I Genital chancre	5	1.32	18 days	Lesions disappeared after 5th treatment. Induration still present.	1 plus	not taken
5	M	20	II Annular	4	1.38	16 days	Lesions disappeared after 4th treatment.	4 plus	not taken
6	F	24	III Nodular	5	1.80	44 days	Lesions disappeared after 5th treatment.	4 plus	1 plus
7	F	18	II Papular. (Moist pap. about vulva)	5	1.68	42 days	Lesions disappeared after 5th treatment.	4 plus	2 plus
8	M	21	II Papular. Mucous patches	4	1.36	42 days	Lesions disappeared after 4th treatment.	4 plus	doubtful
9	M	26	II Pap. pustular	10	4.21	73 days	Lesions disappeared after 10th treatment.	4 plus	negative
10	F	16	II Papular	5	1.72	34 days	Lesions disappeared after 5th treatment.	4 plus	doubtful
11	M	22	I Genital chancre	5	1.82	28 days	Lesions disappeared after 5th treatment. Induration still present.	negative	not taken

TABLE II—CONTINUED

INTRAVENOUS INJECTIONS OF SULFARSENOL

NO.	SEX	AGE	TYPE OF ERUPTION	NUMBER INJECT.	TOTAL AMOUNT IN GRAMS	DURATION OF TREAT.	CLIN. RESULTS	WASS. BEFORE	WASS. AFTER
12	M	17	I-II Chancre (forearm) papular	8	3.48	25 days	Lesions disappeared after 6th treatment. Induration still present after 8th treatment	4 plus	2 plus
13	M	24	II Annular	3	2.04	16 days	Lesions disappeared after 3rd injection.	4 plus	2 plus
14	F	20	II Condylomata	3	1.08	14 days	Lesions disappeared after 3rd treatment.	4 plus	3 plus
15	M	20	II Papulopustular	6	1.88	35 days	Lesions disappeared after 6th treatment.	4 plus	3 plus

very little discomfort. When this dosage, however, was exceeded the patients complained of marked soreness for a period of two to three days, interfering with the movements of the arm (the region chosen for injections). There was also a moderate amount of local tenderness at the site of injection, when the patients returned to the clinic three or four days later. On two occasions there was some induration varying from one to two inches in diameter; the duration could not be ascertained as these patients did not return.

As a result of a limited experience with sulfarsenol, I would conclude that in equal dosage it compares favorably with neoarsphenamine in causing the disappearance of cutaneous lesions. The drug can be employed to advantage in those whose veins are extremely small or too deeply situated to be of value for intravenous medication. The subcutaneous method is not a painless one, it causes considerable discomfort but much less than when used intramuscularly.

PARESIS WITH NEGATIVE SPINAL FLUID

By James Wynn, M.D., Indianapolis, Ind.

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CLINICAL teachers of wide experience are repeatedly cautioning that the evidence of the laboratory, unless supported by clinical data, is rarely sufficient for accurate diagnosis. Especially is this true of syphilis. On the wards of almost any large teaching hospital one may hear, often enough, some such remark as, "This is syphilis, even though the Wassermann reaction be negative." And in a very considerable number of instances subsequent developments establish the accuracy of the assertion.

The cytological, serological, and chemical study of the cerebrospinal fluid at regular intervals furnishes one of the most accurate indices as to what prognosis may be ventured for any neurosyphilitic undergoing treatment. This seems reasonably clear from the observations of Fordyce,[1] Ogilvie,[2] and others.[3, 4] Accordingly, in treating neurosyphilitics some men are satisfied to be guided in their therapeutic program principally by the variations in the cerebrospinal fluid, and have perhaps been prone to be less keenly observant of the clinical changes in the patients themselves. Such practice may lead to grave and embarrassing errors in prognosis. The two cases abstracted in the following illustrate clearly the prognostic importance of critical clinical observation, even though the cerebrospinal fluid variations with treatment may seemingly warrant unqualified optimism.

Case 1.—A policeman, forty-nine years old, with a history of chancre some 25 years before, had had fifteen intraspinal treatments with arsphenaminized serum before coming under observation, and during these injections an elevated cell count had become normal and a Wassermann reaction positive with 0.2 c.c. of cerebrospinal fluid, had become only weakly positive with 1.6 c.c. The blood Wassermann reaction had become negative.

When he came under the writer's observation (several months after the mentioned series of intraspinal treatments) lumbar puncture showed a cell count of

18 lymphocytes per c.mm., a strongly positive Pandy reaction,* and a Wassermann reaction positive with 0.5 c.c. On further intravenous and intraspinal treatment the Wassermann reaction and cell count, as with the previous series of injections, began to show consistent improvement.

The only physical signs were hyperactive reflexes and very sluggish pupillary reactions. From the beginning the patient's only complaint had been sensations of heat waves passing over him. This symptom never changed, even during the periods when under treatment the cerebrospinal fluid approached normal. Well toward the end of the final course of intraspinal treatment, when the fluid showed no abnormality as judged by the usual standards except a very weakly positive Wassermann reaction (with no less than 1.5 c.c. of fluid), he developed clinical dementia paralytica—grandiose ideas, convulsions, and a rapidly progressive dementia.

Case II.—A thirty-seven-year-old musician, with a history of chancre locally treated in youth, complained of headache and paresthesias of one foot. The left knee jerk was exaggerated, the Romberg slightly positive, and the pupils unequal. Wassermann reaction of the blood was positive and of the cerebrospinal fluid positive with 0.3 c.c. The cerebrospinal fluid cell count was 20 and the Pandy reaction positive.

After a year of intravenous and intraspinal treatment according to the general scheme of Fordyce[1] the Wassermann reaction in the blood became negative and in the cerebrospinal fluid negative with all amounts up to 2.0 c.c. The pleocytosis and Pandy reaction also disappeared.

During the year the headaches disappeared, but memory defects and a slight personality change became apparent. The paresthesias remained unchanged. Paresis (persecutory delusions, convulsions, and periodic maniacal outbreaks) eventually developed, though routine chemical, cytological, and serological findings in the cerebrospinal fluid at the time suggested no abnormality.

Fordyce[6] has remarked that the classical signs and symptoms of tabes dorsalis may occur with negative cerebrospinal fluid and blood. In an excellent paper Solomon and Klauder[7] have enumerated, as forms of neurosyphilis in which the cerebrospinal fluid may be negative, certain vascular types, tabes dorsalis, cranial gumma, cerebral nerve palsies, spastic paraplegia, luetic epilepsy, etc. They point out that negative fluid in tabes may mean an incipient case, a treated case, or a spontaneously "burned out" case.

The cases here reported would seem of especial interest in this connection, since the clinical picture of dementia paralytica developed in the course of intraspinal treatment, at a time when the cerebrospinal fluid in each case had become negative. The significant fact is, that while the fluid changes suggested improvement, there were no accompanying clinical evidences of improvement.

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*All cerebrospinal fluid globulin tests were either Pandy or Ross-Jones, as the writer had at the time had no experience with the much more desirable quantitative method recently described by Ayer and Foster.[5]

CONCLUSION

The conclusions seem warranted, that in neurosyphilitics treated by the intraspinal method, the disappearance of pathological reactions in the cerebrospinal fluid is not in itself enough to warrant an unqualifiedly favorable prognosis. The clinical picture of dementia paralytica may supervene, even when the cerebrospinal fluid is negative. In fact, this is merely another evidence of the important truth, too likely to be forgotten in an age of precision instruments and methods, that in critical case study the place of laboratory methods is in augmenting, not replacing, careful history taking and physical examination.

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III. MERCURY INHALATION THERAPY OF SYPHILIS—SHALL IT BE CONDEMNED?*

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THE treatment of syphilis by mercury inhalations has lately received most unfavorable comment and criticism.[1] In a recent exhaustive presentation Cole, Gericke and Sollmann[2] not only strongly advise against the use of the method but even condemn it. Many of the arguments in support of their contentions appear, upon the surface, to be sound and irrefutable, and, in the absence of experience to the contrary, may well seem to be based upon solid, undeniable facts. But upon closer study and analysis their reasoning is found to rest upon faulty premises. As the matter concerns the condemnation of a time-honored remedy, it seems imperative to be reasonably cautious in acceding to their proposed step and discarding mercurial inhalations in the treatment of syphilis. Hence, a careful review of all their condemning and disqualifying evidence with an open and unbiased mind seems very necessary, notwithstanding the apparent validity of the claims and the eminence of the advocates.

Mercury inhalation therapy has been in use by many of the peoples of Asia and Europe for centuries. It has been employed in innumerable cases with results which, for all we know, may have been equally as good as those achieved in modern times, with all the innovations and refined methods of drug administration. The discarding of so old, well-tried and extensively used a therapeutic measure is not a light matter either to the clinician or the scientist. The practitioner who has on numerous occasions resorted to mercury vapor in the cure of his syphilitic cases and is familiar with its many laudable features, will demand strong corroboration of submitted evidence and indisputable proof of the uselessness and dangers of the treatment before he will abandon an accustomed remedy which, for legitimate reasons, may often be his favorite one. If, however, the evidence submitted proves to be disqualifying and condemning and the method really as useless if not as dangerous as Cole, Gericke and Sollmann maintain, then the clinician must relegate his mercurial inhalation therapy to the heap of other discarded remedies and the sooner the better. But does the evidence so far produced justify condemnation? Are the data offered really sufficiently conclusive and convincing? These are the questions which I purpose to discuss; I believe it can be shown that the condemnation of mercury inhalation is unjustified.

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*Read at Symposium on Syphilis, Brooklyn Diagnostic Society, May 12, 1922.

In my early years of general practice I had the privilege of supervising and treating numerous cases of syphilis. I used mercurial vapor therapy very extensively; our present methods of mercury administration and the arsphenamine preparations were not then in existence. Mercury was then chiefly administered orally and by inunction; the intramuscular and intravenous methods were hardly known. In many of my cases oral administration was impossible because of obnoxious gastrointestinal symptoms, thus necessitating the resorting to extraoral methods. Inunctions with 50 per cent blue ointment, or occasionally with calomel ointment, were the next favorite remedy. But inhalations and fumigations were in greater demand because of the objectionable features connected with inunctions. Patients often revolted against these on account of the laborious work connected with the rubbing in of the ointment and the soiling of clothes and bed linen; besides inunctions also exposed the nature of the affliction to all and sundry. Therefore inhalations being free from these undesirable features, were in considerable demand.

My clinical experience with mercury inhalations does not coincide with those recorded by Cole, Gericke and Sollmann; my results were much more satisfactory. I am of the opinion that these authors have not accorded full justice to this method; its faults have been conspicuously presented, while its commendable features have not been sufficiently emphasized. Mercury inhalation therapy, like every other therapeutic procedure, may have certain faults and disadvantages. But are these faults more serious than those of any other mercury therapy? Are they so bad and incorrigible as to demand the total elimination of the whole method?

Are the objections set forth by these authors insurmountable? Let us see whether a careful analysis of all the evidence submitted will justify the condemnation of mercury inhalations in the treatment of syphilis, as propounded by Cole, Gericke and Sollmann.

CONCLUSIONS OF COLE, GERICKE AND SOLLMANN

Passing over the unfavorable survey by these authors of the history of mercury inhalations[24] to which reference has already been made in another paper, let us first proceed to analyze *the conclusions* drawn from their literary review and their own somewhat meager clinical studies on the subject. One of their conclusions is that: "Inhalations and fumigations have always been abandoned as of uncertain efficiency and occasional high toxicity."

I shall in answer to that say, first of all, that the treatment has not been totally abandoned; and, second, wherever it was relaxed, this was done for reasons other than inefficiency and toxicity of mercurial vapors.

Leaving out of account, for the present, ancient times, when mercury inhalation is said to have been practiced in China and India, let us consider the sixteenth century, when syphilis began to ravage Europe. We have abundant records of the popularity of inhalations among many of the great practitioners of that time. Astruc[3] relates that all the chief physicians of that period used mercury inhalations. The method was in truth unsatisfactory and often proved dangerous, but not because of the drug itself but rather the manner of its administration.

First of all, the vaporized mercury was mixed with so many irritating and toxic substances that at times the treatment had to be interrupted or discontinued. These toxic and irritating substances were, we all know, the sulphur which made part of the mercury compound, cinnabar; minium, which was likely to produce lead poisoning symptoms, and a multitude of aromatic substances, "perfumes," that when burned gave rise to irritating fumes. In short, the vapors were suffocating, poisonous and violently irritating. Even calomel, which was also one of the sources of mercury vapor, was volatilized in the dry, giving off obnoxious hydrochloric acid fumes. Still, many patients succeeded in bearing the treatment, and the mercury action took place in spite of prodigious counterbalancing forces, although its specific effect was much offset by the obnoxious and toxic action of the added substances.

In the second place, the inhalations and fumigations were preceded by a ceremonial that in itself was sufficient to reduce the strength and even cause the death of feeble patients. Sweating, purging, bleeding, were preliminaries of every course of mercury treatment before the actual fumigations were administered with, what may without exaggeration be described as a maximum of badness; the patient, quite naked, was placed in a tent and subjected to hot and suffocating fumes until he was in a profuse sweat and half asphyxiated, and only if his suffering became unbearable was he allowed a few mouthfuls of fresh air.

All these procedures tended to lessen the value of mercurial inhalations; they caused it to be doubted, reviled and feared, and often to fall into disrepute. There were many adverse critics who recorded their disapproval in a voluminous literature. But there were also numerous adherents of the method, for, in spite of all, its wonderful curative results could not be dismissed nor permanently overlooked. This accounts for the periodic revivals and the survival of mercury inhalation therapy even to the present day.

If we compare the sixteenth and seventeenth century European method of mercury inhalation—a combination of inhalation and fumigation—with that used for centuries and continuing to this very day in good standing—the Asiatic, a pure inhalation system—if we compare these two methods, we may comprehend why in the East inhalations are still in use in the treatment of syphilis. There, simple inhalations of mercurial fumes, generated by smoking pipes, is still practiced; by this means a considerable quantity of mercury is conveyed to the lungs without cutting the patient off from an intermittent supply of fresh respirable air as happened in the European method; consequently inhalations are still preferred there to every other mercurial administration.

Polak,[4] a German physician long resident in Persia, says that Persians seldom seek the services of the European physicians who treat syphilis by modern methods, but go rather to native quacks, men and women, to be treated by inhalations. These have their special formulae, with cinnabar as the important ingredient. The cinnabar is mixed with tobacco and smoked from pipes once or twice daily; pills containing arsenic are also sometimes given by the quacks but very rarely. Polak also states that though acquired syphilis is frequent in Persia congenital syphilis is rare. He ascribes the infrequency of transmission of this disease from parent to offspring to the common and permanent cure of syphilis by inhalation; this statement so far as I know, has never been contradicted; if true it speaks volumes for the method.

In Europe and our country the mercury inhalation therapy, though neglected since the discovery of salvarsan and the introduction of the hypodermatic use of mercury, has not been abandoned; on the contrary, it is still quite popular and promises to become even more so, as may be judged from its extended application in institutions and by individual syphilologists. Still, its general use is as yet restricted because the objectionable features have not been altogether eliminated.

The contentions of Cole, Gericke and Sollmann that mercurial inhalations have been completely abandoned because of doubtful efficacy and toxicity is not entirely sustained; it is true only insofar as it concerns the long abandoned, antiquated European methods used in certain localities and does not apply to the other methods or places where inhalations are employed in a proper manner.

Another of their conclusions states that:

"The unsatisfactory results are due mainly to the uncertain dosage. Local injury to the lungs is an additional factor."

While this is partly true, it nevertheless calls for explanation and modification. The first part of the statement seems to imply that if the dosage could be made definite, the results would not be unsatisfactory, or, at least, only partially so. This is evidently based upon the assumption that mercury vapor is absorbed in the respiratory tract,—a conclusion which seems to be contradicted in other paragraphs of their paper—in which the authors altogether deny, quite wrongly, I am sure, the absorption of mercury by the lungs. But of that later.

I willingly concede the justice of the criticism of mercury inhalations on the score of indefinite dosage. Any drug of such potency as mercury, no matter how useful a therapeutic agent it may otherwise be, has, if incapable of being administered in definite dosage, and thereby regulated in its pharmacologic action, a serious drawback to its use. "It is a proper postulate of all drug therapy that a precise mode of physiologic action of the agencies employed and their effect on the various parts of the organism must be ascertained as fully as possible before the treatment instituted can be said to rest on a thoroughly rational, scientific basis.''

The methods of generating and administering mercury vapor formerly in vogue sadly lacked accuracy and exactness of dosage; the vaporization technic was crude and the manner of administration, to say the least, was cruel. The placing of a patient under a canopy or in a cabinet, either with the head exposed or enclosed, and subjecting him to mercurial vapors in unknown amounts and generated in some uncontrolled manner, was a very poor procedure indeed, and, from a scientific standpoint, deserves condemnation. Under such circumstances the dosage of administered vapors was very indefinite; at one time the vapors perhaps, never reached the lungs; at others, so much might have been inhaled as to make their absorption dangerous, both circumstances being a discredit to the system of administration.

However, indefinite dosage is not a fault of the inhalation method alone; in every method of mercury administration—oral, intravenous or cutaneous—we are hampered by our inability to ascertain the exact amount of the drug absorbed into the system. Who can definitely tell how much of a dose of mercury administered orally is actually conveyed into the circulation and how much of it passes out unused? Who will presume to estimate what portion of an intramuscular injection entered the blood current and what percentage remains in the infiltrated tissues at the site of injection? The intramuscular method is particularly subject to uncertainty. I may cite in this connection one of many instances observed by me where mercury intramuscularly administered remained unabsorbed for a long time. A very fine, cultured woman who had been unfortunately infected with syphilis by her husband came some time after his death for advice concerning a number of hard lumps in the gluteal regions, where she had previously received intramuscular injections. She wished to remarry but felt restrained from doing so because of the condition of these parts, as it might expose her previous infection, which she was anxious to conceal. Several of these hard infiltrated lumps were excised and found to consist of fibrous and fatty tissue incapsulating the mercury introduced there many years previously and remaining unabsorbed since its injection. Many similar cases might be cited, as the experiences of other clinicians will bear me out, in proof of the unreliability of intramuscular mercury absorption. All other methods of administration of this drug are similarly guilty from this point of view.

Exact dosage is perhaps one of the most important problems with which we are still confronted in mercury therapy. I shall not here attempt to decide whether or not uncertain dosage plays a greater rôle when the method is inhalation or when it is inunction or injection. I recognize the inadequacy of our present methods and to that extent I freely sustain these authors in their criticism of mercury inhalation. To overcome this deficiency of the inhalation method—the indefinite dosage—I have lately given careful study to the generation and administration of the vapors and I believe I have succeeded in perfecting an apparatus by which the dosage of administered vapors may be determined with great exactness. This apparatus,[25] which during the past year has been in practical use here and elsewhere, assures accurate administration and completely eliminates, I feel confident, the question of indefinite dosage in mercurial inhalation therapy.

As to the other part of the second conclusion—that mercury vapor causes local injury to the pulmonary tissues, it seems for the present a sufficient refutation of this to call attention to their own observations described by these writers in the paper under consideration. The authors state in their clinical reports that when inhalations of vapor from *metallic mercury* were given, *neither local nor systemic results were produced,* but with calomel they observed bronchial irritation. This goes to prove that something besides the mercury atom—the chlorine element of the calomel molecule, is the local irritant.

In the older literature many cases of respiratory complications attending inhalations of mercury are mentioned, but in all these it appears that combinations of mercury were used and not the pure metal. Nowhere was I able to find a record of serious respiratory symptoms attending the inhalation of vapors obtained from pure metallic mercury. In our experiments[5] it was found that unless the pure mercury vapor was administered in very concentrated form, without free access of air, or unless it was crowded to extremes (very frequent administration and large doses) there were no exceptional pathologic changes discoverable in the lungs; the findings there were ordinary—moderate congestion, mild shedding of alveolar epithelia, bronchial congestion—and corresponded to the findings in other organs of the animals so treated.

It may therefore be stated that vapors from pure metallic mercury if properly administered are not harmful to the respiratory tract and that uncertain dosage is not an irremediable factor in the use of mercurial vapors.

In their third conclusion the authors say:

"The assumption that mercury would be more promptly absorbed by the lungs was based on physical misconception. In fact the mercury is condensed on the mucous membranes of the mouth, pharynx and respiratory tract. That in the mouth and pharynx is, for the most part, swallowed. The absorption then takes place by the gradual conversion of the mercury into soluble compounds, just as it does with the ordinary administration of 'gray powder.'"

These arguments seem to question the very physical laws of vapor absorption. Mercury in vaporized form is subject to the same laws as other vapors and gases. There is no reason why air filled with mercury vapor and free from other substances inducing respiratory spasm should be condensed on the mucosa of the mouth and pharynx and not pass into the lungs when inhaled. Nor would it on the score of temperature be at once condensed into liquid particles in the mouth, pharynx or upper respiratory tract, for mercury vaporizes at very low temperatures (–39° C.), even below its freezing point. Furthermore, in normal nasal respiration the air is not likely to enter the mouth and cause mercury vapor which it contains to be deposited on the buccal mucosa. This would happen only if the air contained substances offensive to the respiratory tissues, causing spasm and compelling mouth breathing. This must have been a constant occurrence in the long obsolete treatment by "perfumes," as the early fumigations were called; the smoke of the resins, balsams and various other kinds of incense, the sulphur fumes from cinnabar and the chlorine gas from calomel, were each and all competent to produce spasm of the respiratory tract, and consequently mouth inhalations. It is probable that whatever mercury was absorbed in those early treatments, it passed through the buccal mucosa and that the imperfect vaporization of the drug allowed many large not readily absorbable globules of mercury to be deposited in the mouth, producing there the nearly constant and aggravated stomatitis and gingivitis described by the older authors. In the East where relatively pure vapor was employed and inhaled through pipes, neither salivation nor gingivitis was often complained of.

It may thus be safely assumed that under normal circumstances, i.e., nasal inhalation of nonirritating gases, mercury vapor does pass into the lungs, and not into the upper gastrointestinal tract, an assumption directly verified by experimental data and rendered practically certain by clinical accounts.

Let us next consider the matter of absorption of mercury vapors in the lungs. Merget,[6] whose classical investigations published thirty-four years ago have not yet been superseded, showed experimentally that mercury absorption in the lungs is not "based on physical misconception." He proved the presence of mercury in the lungs of animals which he had caused to breathe air containing mercury vapor; he likewise showed that mercury vapor passes through the surviving amphibian lung, a structure which corresponds approximately to a single mammalian air sac, with great ease and swiftness. He also found that mercury vapor diffused in water in which carp were living was effective and even toxic, though he found the toxicity to be less in aquatic animals than in air breathers. This proves that mercury vapor is absorbed even when dissolved in water.

EXPERIMENTS PROVING THE ABSORPTION OF MERCURIAL VAPORS

In order to determine whether all the mercurial vapors generated by the combustion of a suitable mercury preparation are really absorbed if inhaled these experiments were undertaken. An apparatus (see illustration) consisting of a celluloid mask to which a semicircular tubular glass attachment with inspiratory and expiratory divisions was fastened was devised. To the mask direct a T-shaped metal pipe was connected, at either end of which a flutter valve was placed in such a manner that at one end only inspired air could be admitted, while at the other end the expired air was released. A Pyrex tapering cylinder, attached to the outer side

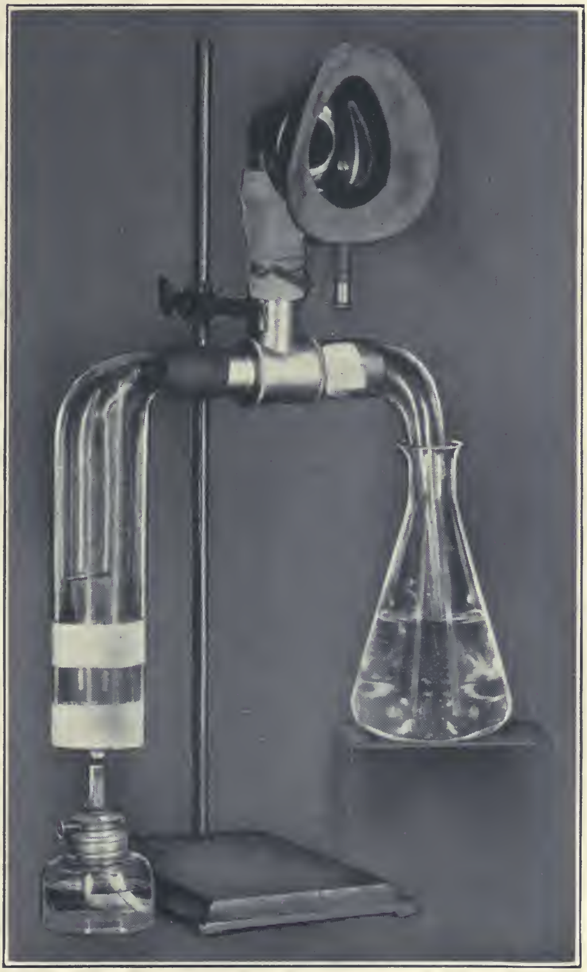

Fig. 1.

of the inspiratory flutter valve, contained a little metal basket intended for the preparation to be volatilized; at the outside of the expiratory side the tapering glass cylinder was introduced into an Erlenmeyer flask containing water or nitric acid solution.

A mercurial preparation consisting of pure metallic mercury mixed with an oxidizing agent and inert organic substances to facilitate combustion, made into the form of a troche, or wafer, was placed in the metal basket and ignited over a Bunsen or alcohol lamp flame. The rubber-cushioned inhalation mask was then placed tight against the patient's mouth and nose so as to prevent loss of vapor at this end of the apparatus. All the vapors generated were thus inhaled by the patient, inhalation being continued until the wafer was completely burned, and its ashes free from mercury. The expired air was made to pass through the other end of the apparatus and through the liquid within the Erlenmeyer flask. All exhalations were thus compelled to go through the liquid and bubble to its surface.

In twenty inhalation tests in which twenty grams of mercury were utilized in the experimental wafers only one tiny globule of metallic mercury was found in the water on the bottom of the Erlenmeyer flask, while in another series of eighteen inhalations only traces of mercury were found upon analysis of the nitric acid solution through which the exhalations had been made to pass. The only other mercury remaining in the apparatus in these two series of experiments was found in the smoky deposit on the inner surface of the inspiratory division through which all the mercurial vapors generated had to pass to be inhaled. After rinsing this division with a nitric acid solution and analyzing the liquid it was found that it contained only about 1 per cent of the total mercury vaporized and having passed through this compartment.

These findings showed conclusively that except for 1 per cent all vapors of mercury released by combustion of the wafers were retained within the inhalers' ororespiratory tracts and that none was exhaled. Such retention makes its complete absorption practically a certainty.

In my experiments on animals subjected to inhalations of its vapors, mercury was found by chemical analysis in every pair of lungs examined. It was also found that when guinea pigs were subjected first to inhalations of dense fumes of mercury and immediately after to those of iodine, a deposit of mercuric iodid throughout the lung tissues had taken place, thus proving that mercurial vapors invade even the deepest part of the respiratory tract.

ABSORPTION OF VAPORS

If it be admitted that mercury vapor does penetrate into the deep lung structures, then why should it not be absorbed there? The structural, physical and functional conditions in the lungs offer facilities for absorption not elsewhere duplicated in the body. Its surface area alone is already a great factor. According to Reichert[7]—"It is estimated that the alveoli number about 725,000,000 and that the total superficies exposed by them to the gases in the lungs is about 200 square meters, or from 100 to 130 times greater than the surface of the body (1½ to 2 sq. meters). The walls of each alveolus form a delicate partition between the air in the lungs and the intricate network of blood vessels. This network is so dense that the spaces between the capillaries, as a rule, are smaller than the diameter of the vessels. The lungs, therefore, are exceedingly vascular and it is estimated that the vessels contain on an average 1.5 kilograms of blood. Owing to the minuteness of the capillaries and the density of the network, the air cells may be said to be surrounded by a film of blood which is about 10 mm. in thickness and has an area of about 150 sq. meters." See[8] estimates the number of alveoli at 809,500,000 and the respiratory area as 81 sq. meters or 54 times as great as the surface of the body.

It is evident that such an enormous surface area provides for extensive contact between inhaled gases and the volume of blood in the very dense capillary network of the lungs. The absorbed air or mercury vapor is rapidly transported into the systemic circulation by means of the large quantities of renewed blood flowing to the pulmonary circulation; thus a constant low tension of the mercury vapor is maintained in the pulmonary blood, which condition favors its transit from regions of relatively high tension, the alveolar air, into those of lower tension, the freshly supplied volume of blood in the adjoining capillaries.

The separating membrane, consisting as it does of but two layers of flattened epithelium and extremely permeable for gases, is another factor favoring pulmonary absorption; it offers a minimum of resistance to the passage of gases and mercury vapor. In Merget's experiment its transit through the frog's lung was so rapid that he spoke of it as "instantaneous." Culbreth,[9] in describing the absorption of vaporized drugs, says—"Vapors of liquids or solids are inhaled with the air, thereby bringing the system quickly under the drug influence; this quick action is due to the rapid absorption owing to the extensive surface of the lungs, etc., to which applied and to the fact that volatile substances penetrate tissues most readily, most vapors at all ordinary temperatures, others at body, while many have to be heated. Most anesthetics act by this method."

Another fact concerning the absorption of mercury is that its vapors, like other soluble vapors and gases, are subject in the blood and alveoli to the laws of specific diffusibility and pressure of gases. The state of general narcosis, for example, is governed by these factors and is not dependent either upon the amount of anesthetic or the period of administration; it is the rate of absorption, in accordance with the crowding of the anesthetic, i.e., the quantity administered in a specific time which determines its concentration in the alveolar air and blood and its transmission to the nervous system, and thus the state of narcosis. All gases and volatile liquids (oxygen, carbon monoxide, nitrous oxide, marsh gas, chloroform, ether, nitrites, etc.), are subject to these laws, those of diffusibility and gas poisoning, and are absorbed into the blood current only in accordance with them.

But not only do the lungs absorb vapors, they absorb them rapidly; the rapidity with which absorption occurs is often remarkable—instant death following the inhalation of prussic acid may be cited as an example. Immediate absorption following the introduction of large quantities of water into the trachea of living animals as shown by Landois,[10] is another example of quick transudation. Peiper[11] quoted this fact for many other substances. Even blood is absorbed rapidly. Nothnagel found blood corpuscles in the interstitial pulmonary tissues immediately after hemorrhage. In pulmonary edema, in lung hemorrhages of whatever origin, and in recovery from drowning, the absorption of fluids from the alveoli is equally rapid. It follows, naturally, that if the pulmonary tissues permit a rapid and complete absorption of fluids, the absorption of gases, mercury vapor included, would be even more rapid and absolute.

Furthermore, penetration of the alveolar epithelium is not limited to liquids and volatile matter. Even solid particles in mechanical suspension in the air pass through the lungs into the mediastinal structures. Any one familiar with the appearance of the lungs in pneumoconiosis will verify this statement. Dust, coal particles, chalk, iron filings and other ordinary solid matter which fills the atmosphere of manufacturing establishments are common constituents of the pulmonary tissues of their workers. These fine particles penetrate the thin alveolar layer, either through the help of the white corpuscles or by mechanical transfer, and are deposited in the fibrous tissues, lymph channels, lymph glands, etc., of the mediastinal tissues.

Finally, the lung surface also acts as an excretory channel and not only as an absorbing medium. Numerous volatile substances brought to them by other routes find their way out of the system through the lungs, some very rapidly. The injection, for example, of a solution of sulphuretted hydrogen into the ear of a rabbit is followed by almost immediate exhalation of the drug. The exhalation of alcohol by the breath, and of anesthetics during recovery from an anesthesia, of many narcotic and other drugs and of products of digestion, are all familiar examples.

All the evidence,—physical, physiologic, chemical, clinical and experimental,—shows the absorbability of mercurial vapors and the conclusions of Cole, Gericke and Sollmann, who deny to this method of mercury administration the possibility for absorption.

THEIR CLINICAL EVIDENCE

And lastly, little importance should be attached to the clinical evidence submitted by these authors in proof of the nonabsorption and inactivity of mercury vapors. Only six clinical histories are given of patients who received a course of "inhalations with 5 to 160 mg. of mercury to a total of from 225 mg. in two weeks to 750 mg. in three weeks" given through a specially designed tube. It is said that in these cases there were no local or general effects, no salivation, and except in one doubtful case, no sore gums. The completely negative results were followed by prompt improvement when arsphenamine was given.

Since the six patients to whom the mercury vapor was administered through the mouth showed either no symptoms or, in the one case, only slight salivation of doubtful origin, the inference seems inescapable that no mercury was absorbed by these patients. This suggests several possibilities: 1. The mercury was not driven off from the inhalation tubes designed by the authors and into the mouth of the patient. 2. If driven off and condensed in the mouth of the patient, then the mercury was not absorbed, which is contrary to the claims of the authors, who maintain that whatever mercury is absorbed during an inhalation, is absorbed principally after its condensation in the mouth and pharynx mucosa, its conversion there into a soluble form and its subsequent swallowing. 3. If the mercury was driven off from the apparatus and was absorbed, whether from the gastrointestinal or respiratory mucosa, then the dosage calculated on the basis of other methods of mercury administration was inadequate to produce any effect, either curative or toxic.

Since no appreciable results, either good or bad, were produced by these inhalations in the cases cited, we may leave these observations, in any question of the value of mercury vapor as a remedy for syphilis, out of account for the present. Besides, the number of experimental cases cited is so small that little value could be assigned to the results obtained, even had they not been entirely negative.

PHYSIOLOGY OF RESPIRATION

The statement of Cole, Gericke and Sollmann that whenever mercury is absorbed during inhalation, this is accomplished through the deposition and condensation of the vapor in the mouth and adjoining mucosa, is not compatible with facts. They express their conception of what takes place in the following manner: ''The second assumption that inhalation would avoid the local effects on the digestive tract is correct because a considerable part of the mercurial vapor is condensed on the mucous membrane of the mouth and pharynx and is gradually swallowed with the saliva. The proportion that thus goes into the digestive tract doubtless varies with conditions; but it must be considerable, and may well be the major part.''

First of all, these views are contrary to their own statements.

In the earlier chapters of their thesis they quote many historical instances where mercury vapor inhalations caused definite lung affections. If, as they claim, inhaled vapors do not penetrate into the deep alveolar structures, how then would the pulmonary parenchyma be so affected as to become the site of very profound pathologic lesions? On the other hand, if the vapors produce lesions in the deeper lung tissues, then this would constitute proof that the vapors do reach the alveoli.

In the second place, their assertions contradict physiology. This teaches us that inspiration is an active process. The rarefaction of alveolar air, due to thoracic expansion (through muscular action) causes the outer atmosphere, denser and under greater pressure, to be drawn in and to diffuse through the rarefied air in the respiratory tract. The air inhaled through the normal channel, the nose, takes a definite course; it does not enter the closed digestive tubes whose walls are normally in apposition, but the current is drawn into the open respiratory tube whose air is rarefied. Even if some of the current enters through the mouth channel, it reaches only the oropharyngeal space under ordinary circumstances and does not pass into the deeper alimentary canal; whereas, in its normal course, the inhaled air or vapor fills all nooks and corners of the nose, nasopharynx, sinuses, etc., and then invades the deeper respiratory tract. In the upper chambers its temperature is increased; it then becomes saturated, if not already so, with aqueous vapor, deposits its dust particles upon the mucosa lining the irregular walls and frees itself from pathologic bacteria by its contact with the antiseptic nasal secretions. Every volume of inhaled air, gas or vapor thus comes into touch with the large area of respiratory mucous membrane, where it lingers and where its local absorption is undoubtedly favored even before it reaches the alveolar spaces. Even admitting that a part of the inspired air or vapor does come into contact with the digestive mucosa, this must necessarily be so insignificant compared with the large volume admitted into the respiratory tract that it would have but little bearing in its effect upon the general organism compared with the effect of the inhaled volume and it may be quite ignored; it is only if the inhaled substance is found by the delicate olfactory and sensory filaments to be of an irritating character and is expelled by the reflex mechanism of coughing or sneezing, that a person who is still compelled to breathe obnoxious vapors, through the mouth, may swallow them in considerable amounts. Under these circumstances considerable quantities of the inspired substance may reach the digestive mucosa and become absorbed there. Since pure mercury vapor is not irritating it stands to reason that in ordinary respiration the greater part of the air containing mercury vapor would be drawn into the rarefied area of the expanded lung and would not be forced into the normally closed digestive tube. Hence, greater absorption and greater subsequent effect upon the organism may naturally be attributed to the mercury reaching the respiratory tract, than to the small fraction that may come into contact with the buccopharyngeal mucosa, even if some mercury is deposited there and swallowed, as Cole, Gericke and Sollmann maintain.

IS THE ADMINISTRATION OF DRUGS BY THE PULMONARY ROUTE RATIONAL THERAPY?

This question has lately been raised in connection with mercury inhalation.[12] Doubt has been expressed as to whether the administration of drugs by the respiratory tract for constitutional effects is rational therapy, and whether medicinal preparations specially designed for this purpose should be considered therapeutic agents.

It seems nearly axiomatic to state that any part of the body capable of absorbing and delivering into the general circulation a remedial agent may be utilized as a route for administering such agent. This fact is made use of in every day practice; various bodily organs, including the respiratory tract, are daily utilized to absorb drugs for effect upon the general organism. It would, therefore, seem unnecessary to dwell upon the utility of inhalations. These have long ago established for themselves a permanent and enviable record.

The inhalation of medicated vapors is a procedure long in existence. We need only to recall the common use of the steam kettle, with or without balsams or other aromatics, in nearly every household throughout the world, to prove the widespread use of vapor therapy. Medicated vapors are considered invaluable as a local remedy for their sedative effect upon the respiratory mucosa and as a means to induce secretion, disinfection, dilution of mucus, etc.

Hence, to defend mercurial vapors as a local remedy in disturbances of the respiratory tract seems quite out of place; its reputation there is well established.

Neither do inhalations need to be defended as a constitutional remedy, for it is common knowledge that vaporized drugs are effective upon the general organism. Volatile substances are administered daily for this purpose—anesthetics, antispasmodics, stimulants, nitrates, etc., for example. When nonirritating gases are inhaled they are absorbed from the pulmonary tract, and transported by the blood current to distant organs where they take effect; irritating gases are expelled reflexly. The facilities for rapid and immediate absorption in the lungs, as has previously been shown, are unusual; the opportunities for delivery into the blood stream greater than elsewhere.

What is true of all vapors is true also of mercury whose physical properties make it exceptionally favorable for inhalation and absorption. One of its characteristics is that it volatilizes readily; this occurs not only at ordinary temperatures, but even as low as $-39.4°$ C., i.e. in the solid state.[13] When the temperature is raised to $+5°$ C., it vaporizes quite perceptibly and at 150 to 250 degrees, the smouldering heat at which metallic mercury is ordinarily vaporized, the process is much accelerated. Vaporization is even more complete when liquid mercury is thoroughly triturated with oxidizing agents or combustible organic matter; its conversion into vapor is then rapid and complete.

As to the question whether mercurial vapors affect the organism, argumentation is unnecessary. The evidence—clinical, experimental, pharmacologic, toxicologic, etc.—is so preponderant that to dwell upon it would be superfluous. Cases too numerous to mention are recorded in the literature of mercurial poisoning having occurred even through the slow inhalation of its vapors. The experience of clinicians and research workers who employ the vapors testifies to its effectiveness and absorption. Perhaps a few of many opinions on this subject may be quoted:

"There can be no doubt regarding the possibilities of bringing about absorption of mercury introduced into the body in the form of vapors. Numerous records of actual poisoning through inadvertent exposure to atmospheres in which mercury was present attest the potency of the vaporized element." (Sollmann.[14])

"The mercury compounds are absorbed from all surfaces. On this rest the mercurial treatments by fumigation and inhalation. Many cases of mercurial poisoning have also been caused by flushing out large cavities with mercuric solutions. The absorption from serous surfaces is also very rapid." (Cushney.[15])

"Mercurial vapors have a great power of diffusion quite comparable to that of other elastic fluids; this permits the point of toxic action to be at a great distance from the place of admission." (Merget.[16])

"Mercurials are absorbed from the alimentary tract and when injected from all cavities and tissues of the body." (Wilcox.[17])

"It is also possible for the vapor to be absorbed by the mucous membrane of the lungs, and this pulmonary absorption of the lungs is not at all uncommon when mercurial preparations (many of which are very volatile) are applied to the skin."[18]

Considerable other evidence might be adduced as proof that mercury vapor *is* absorbed by the lungs and does affect the general organism. The respiratory tract must therefore be accepted as an avenue of drug administration. This being so, suitable pharmaceutical preparations specially adapted for administration through the respiratory tract are as much in place as preparations designed for use through other parts of the organism, such as rectal suppositories, hypodermic ampules, troches, etc.

MERCURY IN THE CIRCULATION

The form in which mercury administered by any route circulates in the blood is still an unsettled question. A number of theories have been advanced but none seems to have sufficient support to warrant a final acceptance. Witthaus[19] says that "Elementary mercury administered by mouth is probably insoluble in the digestive fluids and only becomes active if converted into its oxide form. It is in this form that the metallic mercury of the few U.S.P. preparations presumably become active." He also states that "insoluble preparations of mercury are absorbed in the form of albuminates, and even the metal may become oxygenized and absorbed when it is applied to the living surfaces or injected into the blood in a state of fine division."

Mialhe, Overbeck and Gubler[20] claim that when mercury reaches the blood it forms mercury albuminates and oxalbuminates. Lewald, Michaelis, Hermann and Kirchwasser maintain that mercury droplets are deposited on the mucosa and are oxidized and transformed into oxyalbuminates after penetration into the blood. Rabuteau[21] believes mercury circulates in the metallic form. Nodwagel and Rossbach[22] believe its absorption occurs partly as a salt and partly as a metal. Fuhrbringer[23] in summing up previous investigations, concludes that mercury is deposited on the pulmonary mucosa which it cannot traverse except when this is injured (Rindfleisch); and when this is not the case, as frequently happens, the mercury is oxidized and transformed into resorbable products. Furbringer believes that the mucous membrane causes condensation of the mercury simply by a difference of temperature and that the tension of the mercury vapor is too low to permit its diffusion. Merget counters these assertions by placing a lung over one opening of a two-way mercury flask and testing the reaction at both openings. The reaction was identical at both points, showing that the lung offers a negligible resistance to the passage of mercury vapor. He and others make the following claims: Mercury circulates in the blood as a double chloride and upon reaching the cellular tissues it unites with their protoplasm because of the metal's strong affinity for the nitrogenous element of the molecule.

Metallic mercury in bulk is practically not absorbed and can hardly be considered a poison. The literature contains numerous references to individuals who have swallowed large amounts of liquid mercury with suicidal intent or for obstinate constipation, intestinal obstruction, etc., without serious effects, other than mild salivation or gingivitis. The larger the globule, the less its relative effect; the smaller the droplet, the greater is its absorptive surface and subsequent action. The vapor is the most absorbable and most active form of mercury because of its finely divided state. Hence, freshly generated mercurial vapor, consisting of minutest particles, of molecules with but a single atom, must necessarily be the most readily absorbable form in which metallic mercury may be introduced into the system, and the most active.

From a practical standpoint, the exact form in which mercury circulates in the blood is unimportant. It is an academic question, and as such, of course of great interest. The important practical issue is whether mercury vapor is absorbed, whether it enters into the blood current and is made active in the tissues as an antiluetic factor. These are the points which chiefly interest the clinician.

The unbiased opinion of those familiar with all facts—historical, clinical, therapeutic, etc., would favor mercurial inhalation therapy and not condemn it. Granting even that inhalation of mercury constitutes one of our several imperfect methods of treating syphilis, it should be our task to examine its imperfection and to subject the method rigorously to every essential test so as to determine its usefulness and its limitations and, if possible, to perfect its application. Until we have in hand another method superior in all respects to this one, we should not abandon it; so long as we have not a means of treatment at once more effective, more convenient, and more generally applicable, we need this procedure and our patients need it.

CONCLUSIONS

1. Evidence is presented which contradicts the allegations of Cole, Gericke and Sollmann regarding the utility and effects of mercury vapors in the treatment of syphilis.

2. Evidence is submitted to prove that the respiratory tract is a desirable route for the administration of all drugs effective upon the general organism, especially mercury, because—(a) The absorptive area of the respiratory tract is enormous, many times greater than the external surface of the body; (b) the very dense capillary network of the pulmonary tissue and its immense quantity of blood, renewed more frequently than that of other capillaries, favors immediate transportation of absorbed vapors; (c) the very thin partition (two endothelial cells) between vapors in the alveolar spaces and the blood in capillaries, favors rapid diffusion; (d) the ready vaporization, the nascent state and the peculiar molecular construction of mercury—all favor rapid diffusibility, absorption and effectiveness.

3. Physiological data have been offered to prove that inhaled mercurial vapor is absorbed almost entirely from the respiratory and not the gastrointestinal tract.

4. Evidence has also been submitted which proves that inhaled vapors are not toxic or harmful to the respiratory tract; also that mercury inhalations are still in use.

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IV. MERCURY VERSUS ARSPHENAMINE IN THE TREATMENT OF SYPHILIS

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THE dream of *sterilisans magna* which Ehrlich had entertained in the discovery of salvarsan has not yet been realized. Every syphilographer has learned by now the futility of trying to cure syphilis with salvarsan alone. Arsphenamine is a very marvelous remedy; it often accomplishes the most wonderful and immediate changes in symptomatology, to the great satisfaction of the patient and his attending physician. But unfortunately a final cure is not always attained because the permissible dosage of arsenic, in the present form of the drug, seems, in most cases of syphilis, incapable of destroying every plasmodium in the infected organism without killing, or, at least, injuring the host. It appears that spirochetae, even after a vigorous course of arsphenamine, remain sufficiently resistant to withstand the powerful action of the drug and they acquire a tolerance for it—practically an immunity. As an example of arsphenamine inadequacy I might cite here a case I have in mind in which seventy-eight intravenous and thirty-four intramuscular injections of salvarsan were given, and in spite of this severe, almost unbelievable, treatment, relief from terrific nocturnal headaches of tertiary syphilitic origin was not obtained. It required considerable use of mercury and pituitary extract before this annoying symptom could be eliminated.

Besides, the administration of arsphenamine, in addition to its frequent inadequacy, is not uncommonly accompanied by undesirable complications some of which not only threaten but may even destroy life. It often becomes a serious problem whether, in a particular case, arsphenamine may be employed with safety. The toxicity of this drug is common knowledge, and it manifests itself in a variety of ways; its promiscuous use is to be deplored. Many syphilographers have called attention to its dangers and complications. "The untoward symptoms that still frequently follow the intravenous administration of arsphenamine have been a cause of much concern to therapeutists. Despite the years that have elapsed since this mode of treating syphilis was first introduced as a result of Ehrlich's investigations the difficulties encountered have not yet been overcome."

Chargin[1] states—"That the arsphenamine group of remedies is not devoid of the possibility of serious harm, is demonstrated by the various types of dermatoses, nephritis and encephalitis, neuritis, and nitritoid reactions with their complications which are definitely known as arsphenamine by-effects. And one need hardly mention that there are a considerable number of deaths directly placeable to arsphenamine therapy." Many others have written in a similar vein.

It is not my intention to dwell here upon the bad effects frequently following arsphenamine administrations, but attention *has* to be directed to numerous fatalities reported by many clinicians, in all countries and in numbers not to be disregarded. Minor accidents, such as various dermatoses, plastic anemias, chills, fever, cyanosis, etc., are so numerous as to be considered common coincidences. To mention only a few among many, such accidents have been reported by Milian,[2] Sicard, Paraf and Forestier,[3] Sussig,[4] Jeanselme and Pomaret,[5] Moore and Keidel,[6] Whiteside,[7] Gougerot,[8] Gorke,[9] Stuart and Maynard.[10]

The causes for these serious complications of arsphenamine injections have been laid to many factors: the chemical composition of the drug, the reaction of the solution, its temperature and flocculency, faulty chemical composition of glass utensils, inferior quality of rubber tubing, too rapid administration, the physical state of the patient, his mental habits and thyroidal responses; also microbial endotoxins and numerous similar causes. All these and other harmful possibilities are attributed to arsphenamine therapy by some, though not by all clinicians.

But whatever the actual causes of the complications may be, the faults we must admit are there. Several facts stand out conspicuously and cannot be denied. First, that in many cases of arsphenamine administration very undesirable reactions, from simple dermatoses to conditions resulting in death, occur; second, that in many instances the physical condition of the patient contraindicates its use; third, that arsphenamine alone is not the remedy *per se* and cannot be wholly relied upon as a cure in syphilis; fourth, that mercury, or other drugs, must still be resorted to in the treatment of this disease, whether as specifics or adjuvants.

Mercury still remains the anchor of hope in syphilis. "Mercury like quinine in malarial fever is universally conceded to be a true specific, although its precise mode of action has not as yet been determined. While some authorities have contended that its curative influence is due simply to the general effect upon the metabolism, it seems altogether probable that this is attributable to a specific toxicity for the syphilitic virus which, when the drug is adequately exhibited, finally results in the complete destruction of the latter. Some eminent syphilographers hold that the action of mercury is to clear away from the tissues the products of a specific inflammation, or, at least, to relieve the tissues encumbered with superfluous and obstructive materials; but whether it develops a specific destructive action on the virus or not, the fact remains that mercury is employed in syphilis because experience has shown indisputably that it cures the disease. In order to secure the most satisfactory results it is requisite that its administration should be commenced at the earliest possible moment and that it should be continued for a considerable period after all manifestations of the disorder have disappeared." Wilcox.[11]

Mercury thus retains a most important place in the treatment of syphilis, and if it be admitted that it is still a necessity in the treatment of this disease, then the question arises—what is the best form in which it shall be administered, in quantities sufficient to produce the desired results and in a manner least objectionable to the patient?

Formerly the administration of mercury was by mouth, by inunction and by fumigation; in our time the intramuscular, hypodermic and intravenous methods were added. No one will deny that each of these methods has its particular advantages and that each also has its disadvantages. No method is perfect; none is applicable or practical in every case. No method should be regarded as specific to the exclusion of all others, and none is so completely bad as to warrant its total exclusion from the therapeutist's armamentarium. Each method of administering mercury is useful, practical and applicable in specific instances, and it is for the clinician to decide which one is the best adapted to a particular case. The question of mercury administration in syphilis is not entirely settled; its final chapters are not written, and any new researches with prospects of improving the administration should be welcomed by all.

ADVANTAGES OF MERCURY INHALATION

The newer preparations of mercury, in spite of claims of their low toxicity, blandness, noncorrosiveness, nonirritability, etc., are nevertheless, in actual practice, found not to be as faultless or pleasant as we are led to believe nor as efficacious as desired.

In a previous paper, I made mention of the unpleasantness of the inunction method, its unreliability and indefiniteness of absorption. I also called attention to the painful procedure and the unsatisfactory absorption of intramuscular injections. But even the intravenous method is not without faults; the isotonic, presumably well sterilized and nicely marketed preparations have been accompanied, even in the hands of the experienced, by many untoward by-effects which indicate the need of greater caution in their use. It is not suggested here that inhalations are faultless and that all methods of mercury administration are to be discarded for them, rather is it intended to point out that the other methods are also not faultless and that inhalations, though imperfect as yet, have many advantages deserving attention. First among these, inhalations are free from the nauseous taste and the unpleasant gastrointestinal disturbances occurring with oral administration; second, their absorption is rapid—as rapid as any other method of mercury administration, not excepting the intravenous or subcutaneous; third, compared with inunctions, they have no unpleasant, unesthetic features, such as the soiling of clothing and linen, etc.; they are definite in dosage and absorption; fourth, they never cause serious symptoms or fatalities, such as often accompany hypodermic injections of mercury or arsphenamine; fifth, if administered in proper dilution they cause no unfavorable local symptoms in the respiratory tract; sixth, if administered in a manner devised by the author, the dosage and absorption are absolutely controllable and can be made exact.

On all these accounts it is claimed that the administration of mercurial vapors as compared with the other methods, is comparatively simple, free from pain, discomfort or unpleasantness; in the form of vapor mercury may be administered without disagreeable complications; the vapors are readily absorbed and strongly effective.

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TOXICITY AND TRYPANOCIDAL ACTIVITY OF TARTRO-BISMUTHATE AND ITS RELATION TO THE TREATMENT OF SYPHILIS

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MANY reports have recently appeared in foreign literature giving the results of bismuth in the treatment of syphilis. Our interest in chemotherapy prompted us to study the methods of preparation and determine the toxicity of this product, in addition to an extensive study of the trypanocidal activity of the drug when administered by several routes. We have studied various methods of preparation of the product and established the toxicity on the basis used in testing arsenicals.

CHEMICAL AND CLINICAL

Cowley (1913) at the meeting of the Australian Association for the Advancement of Science held in Sydney, stated that bismuth citrate acts as a monobasic acid giving a well-defined end reaction when titrated with a solution of ammonia. Cowley pointed out that ammonia was not the only base capable of forming a compound with bismuth citrate; all other alkalies behave similarly and it is quite easy to prepare bismutho-citrates of sodium, potassium or lithium by titrating freshly precipitated bismuth citrate with hydroxides, carbonates or bicarbonates of these alkalies. The compound is soluble in water. These ideas were carried out with the use of tartaric acid and the same observations were made as in the case of citrates. The preparation of the sodium potassium compound was carried out by using bismuth subnitrate, 70 grams; sodium potassium tartrate, 64.5 grams, nitric acid (sp. gr. 1.42), 57 c.c. and sodium bicarbonate, 57 grams.

"Dissolve the bismuth subnitrate in the nitric acid diluted with a similar volume of water, add the sodium potassium tartrate dissolved in a little water, then the sodium carbonate also in solution; heat to expel the carbon dioxide; filter, wash the precipitate until free from nitrates. To the washed precipitate, add 230 c.c. of normal solution of sodium hydroxide.

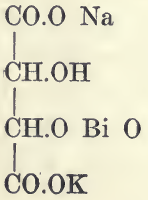
"This forms a perfectly clear neutral solution. For convenience of anyone preparing a solution of sodium bismutho-tartrate the above proportions will make a solution containing the same quantity of bismuth as the liquor bismuthi A.P.F. The alkaline bismutho-tartrates have been recommended for the preparation of bismuth and pepsin mixtures, but they do not appear to possess any particular advantage over the bismutho-citrates and are never likely to take their place in medicine."

"Alkaline Bismutho-racemates.—Racemic acid as might be supposed from its relation to tartaric acid readily forms alkaline bismutho-racemates. They are only of interest in the laboratory.

"Other Organic Bismuth Compounds.—Bismuth malate, bismuth oxalate, bismuth succinate, bismuth phthalate, bismuth camphorate, are all easily prepared compounds of bismuth, but in no case do they form soluble compounds with alkalies. The behavior of bismuth malate towards alkalies is interesting as its relationship to tartaric acid would lead one to anticipate that it would form soluble compounds with alkalies similar to the tartrates."

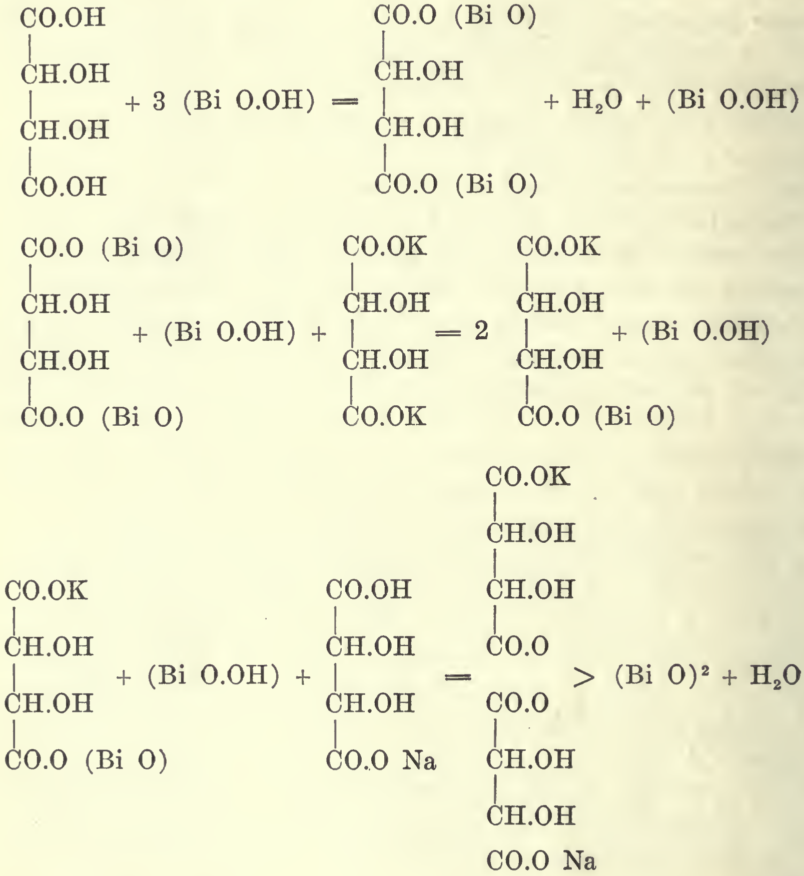
Fabregue (1922) describes the preparation of the citrate and tartrate of bismuth. Dissolve 100 grams of $Bi(NO_3)^3$ in glacial acetic, add 500 c.c. of water and filter. Then add a solution of 67 grams sodium citrate in 600 c.c. of water. Decant the white precipitate and wash it with 90 per cent ethyl alcohol until the alcohol leaves no residue upon evaporation. Dry at about 60°. This product is insoluble in water, alcohol, ether, and dilute acids but soluble in dilute ammonia. The tartrate is prepared in a similar manner.

The composition of the product has received some consideration by several investigators. The constitutional formula



$$\begin{array}{l} \mathrm{CO.O\ Na} \\ | \\ \mathrm{CH.OH} \\ | \\ \mathrm{CH.O\ Bi\ O} \\ | \\ \mathrm{CO.OK} \end{array}$$

has been accepted by a few. In other instances an entirely different point of view has been accepted. Calcagno (1922) has written considerable on this subject and seems to have arrived at a conclusion in which a bismuthic acid is involved and by different methods comes to a conclusion as follows:



$$\begin{array}{l}\text{CO.OH}\\|\\\text{CH.OH}\\|\\\text{CH.OH}\\|\\\text{CO.OH}\end{array} + 3\ (\text{Bi O.OH}) = \begin{array}{l}\text{CO.O (Bi O)}\\|\\\text{CH.OH}\\|\\\text{CH.OH}\\|\\\text{CO.O (Bi O)}\end{array} + H_2O + (\text{Bi O.OH})$$

$$\begin{array}{l}\text{CO.O (Bi O)}\\|\\\text{CH.OH}\\|\\\text{CH.OH}\\|\\\text{CO.O (Bi O)}\end{array} + (\text{Bi O.OH}) + \begin{array}{l}\text{CO.OK}\\|\\\text{CH.OH}\\|\\\text{CH.OH}\\|\\\text{CO.OK}\end{array} = 2\ \begin{array}{l}\text{CO.OK}\\|\\\text{CH.OH}\\|\\\text{CH.OH}\\|\\\text{CO.O (Bi O)}\end{array} + (\text{Bi O.OH})$$

$$\begin{array}{l}\text{CO.OK}\\|\\\text{CH.OH}\\|\\\text{CH.OH}\\|\\\text{CO.O (Bi O)}\end{array} + (\text{Bi O.OH}) + \begin{array}{l}\text{CO.OH}\\|\\\text{CH.OH}\\|\\\text{CH.OH}\\|\\\text{CO.O Na}\end{array} = \begin{array}{l}\text{CO.OK}\\|\\\text{CH.OH}\\|\\\text{CH.OH}\\|\\\text{CO.O}\\ \\\text{CO.O}\\|\\\text{CH.OH}\\|\\\text{CH.OH}\\\text{CO.O Na}\end{array} > (\text{Bi O})^2 + H_2O$$

Other possible means of arriving at the same product are described in the succeeding pages of the discussion by Calcagno.

Robert and Sauton (1916) made a biological study of the tartrobismuthate and found that the hen tolerates 30 to 35 milligrams per kilogram body weight when given intravenously and the animal when infected with spirillosis tolerates only 15 to 20 mg. Intramuscularly, 100 mg. per kilo is tolerated without any reaction by healthy chickens. In the latter case, part of the bismuth is fixed in the form of a white deposit in the tissues where its presence may be detected after 15 days by a drop of sulphydrate of ammonia. In vitro the mobility of spirillosis gallinarum is not lost after three days' exposure to a 1:100 solution of the drug. The same results were obtained in vivo. From a preventative point of view these authors noted a slight inhibition.

Robert and Sauton found that 20, 25, or 30 mg. of bismuth per kilo body weight, will delay the appearance of spirilla for a day if the drug is given intravenously 24 hours before the inoculation. Under the same conditions intramuscular injections of 50-75 mg. per kilo have had an efficacious action. From a curative point of view these investigators believe that as low as 12-15 mg. per kilo prevents an acute development of the disease. They conclude that "the tartrobismuthate of sodium, contrary to the action in vitro, exercises a bactericidal action on the Spirocheta gallinarum in the animal organism. Its action is very effective, for we have been able to prevent and cure infection in a number of cases proportionately high, although this action has not been manifested in our experiments with all the desired regularity. It is due probably to the nature of the bismuth compound used, which loses its effectiveness after its fixation or reduction.

"Our first experiments on preventive and curative treatment of trypanosome affections have shown, with the guinea-pig, comparatively positive action with the use of the following: soluble phosphate, double hyposulphite of potassium and of bismuth, tartrobismuthate of sodium and the ammoniacal citrate."

Sazerac and Levaditi (1921) concluded "that the tartrobismuthate of potassium and sodium has a decided curative effect on experimental syphilis of rabbits (dermotropic and neurotropic virus). The results obtained in the treatment of trypanosomiasis Nagana, though undeniable, are nevertheless inferior to those observed in syphilis." Sazerac and Levaditi (1922) carried out a number of studies on five human subjects with apparent satisfaction serologically and clinically except that stomatitis, salivation, gingival margin resembling a saturnine margin, were observed and they concluded that "Bismuth is a spirillicide of remarkable activity, and its action, as much with man as with animals, is comparable to that of the best antisyphilitic medicaments. It seems to work better than mercury and more effectively, although in certain cases, less rapidly than the most active arsenicals.'' They point out the relative simplicity of its molecular structure and its stability.

Marie and Fourcade (1922) treated twenty cases of neurosyphilis with the drug. No particular results were observed and from the intoxication point of view they noted a slight sensitiveness of the mouth.

Fournier and Guenot (1922) treated two hundred cases with the bismuth salt and noted a rapid disappearance of spirochetes and negative Wassermann in primary and secondary cases. Tertiary cases did not respond serologically. They also state the toxicity of bismuth for the host is low. They regard it as an extremely powerful antisyphilitic agent but caution against the possibilities of stomatitis.

Milian and Perin (1922) state ''We have the honor to present to the Society five patients showing discoloration due to bismuth stomatitis. These patients were treated with the insoluble tartrobismuthate of potassium and sodium in oily suspension, according to the formula indicated by Sazerac and Levaditi. They received intragluteal administrations, 20 centigrams of tartrobismuthate every two or three days, and lesions have appeared after a number of injections which varied for each of them. They show in different degrees two kinds of lesions: lesions of pigmentation, characterized by gingival healing and limited pigmentation; and inflammatory lesions, characterized by gingivitis and ulcerous stomatitis.

''Bismuth stomatitis is not a recent disease. In 1889, M. Balzer (Societe Biologie, 1889) reported the first use of bismuth in syphilis, and experimenting according to Dalche and Villejean (Recherches experim. sur la toxicitie du bismuth. Arch. gen. Med., Aug., 1887) on the effect of bismuth salts injected into the dog showed the existence of stomatitis which seemed to him ought to restrict the field of tentative therapeutics in the case of man. The work of Sazerac and Levaditi has lately made bismuth the order of the day, and the frequency of stomatitis has been stressed at the same time. The work in full has been published by the Societe medical des hopitaux, 1922, p. 135.

''Two factors have seemed to us to compromise the buccal lesions: the medicinal doses used and the previous state of the mouth and teeth. Our observations are taken from a total number of fifty patients, comprising thirty men and twenty women with syphilis at different stages. These patients were treated exclusively with insoluble tartrobismuthate. In the first series with thirty patients, we used a dose on the average of 20 centigrams, repeated every two days, in intramuscular injections in a course of from ten to twenty following the first. After these doses we observed stomatitis with great frequency almost identical in the two sexes.

"Percentage of gingival margin in all of the patients treated.

Margin with gingivitis...........	47 %
Limited ulcerations..............	30 "
Diffused stomatitis..............	6 "

"In a second series of about twenty patients, we used the same dose of 20 centigrams at longer intervals, about every three days. After these doses, the lesions occurred with less frequency and the percentage is as follows:

Gingival margin	95 %
Margin with gingivitis...........	25 "
Pigmented spots	40 "
Limited ulcerations..............	10 "
Diffused stomatitis..............	0 "

"Most of the lesions observed in the second series have appeared less intense and more delayed. Their frequency would be reduced by the use of smaller doses or doses at longer intervals, but it would then be a question whether the therapeutic activity of the product were too diminished."

They examined the pigment and showed that it was bismuth. In the case of one patient, a black urine was excreted in which bismuth was demonstrated.

Carle (1922) states the great obstacle in this medication is the local pain, generally troublesome and radiating in different directions in the region of the injection. "In reality, I have not encountered a single serious accident." Ten patients were treated; three cases of stomatitis, two extremely inflammatory reactions, one oily cyst were reported. Carle does not have a good impression of this drug. However, he concludes that the bismuth preparation is a very strong antisyphilitic remedy.

Jeanselme, Pomaret et al (1922) point out the high toxicity of the drug by the intravenous method and caution against the danger of getting any of the drug into the veins when given by the intramuscular method. They point out that small amounts of the drug intravenously have proved fatal. The results with bismuth are slower than with arsenic and they observed stomatitis in 40 per cent of their cases, depending on the oral hygiene of the patients.

Jeanselme and Blamoutier (1922) report jaundice and a pronounced Herxheimer reaction in two cases which they studied.

Hudelo, Bordet, and Boulanger-Pilet (1922) treated fourteen patients and found a large number of cases of stomatitis even when the oral hygiene was excellent. They state that they find 30 per cent of the cases showing stomatitis; in fact, all the patients without exception have presented, after the first injection, a primary degree of stomatitis characterized by ''a spotted pigmentation, found on the level with the teeth, especially on the lower gum, in the form of a typical blue margin; a certain number of these patients showed on the inside of the face on one or both cheeks a pigmented area, without other modification of the mucous membranes.''

Mueller (1922) confirms the work of Sazerac, Levaditi, Fournier, and Guenot.

Bloch states, ''that we have as yet no reason to suppose that bismuth therapy may replace salvarsan therapy, for, though it acts effectively, clinically and bacteriologically, still it does not reach the efficiency of salvarsan in serological effect. On the other hand, it appears that bismuth is decidedly superior to mercury in activity and tolerability and that, consequently, it is quite possible that in the future bismuth may replace mercury partly, or entirely, in the case of mixed treatment. We have consequently begun recently to introduce such salvarsan and bismuth mixed cures, the results of which are quite excellent.''

TRYPANOCIDAL TESTS

Adler (1921) studied the effect of bismuth in the form of soluble bismuth tartrate in solutions of various strengths on animals infected with T. rhodiense and T. brucei (Nagana ferox). The minimum lethal dose cleared the blood of trypanosomes in a mouse within 24 hours but the animal died in two days. The minimum lethal dose for healthy mice was found to be 47 mg. per kilo of body weight and 62 mg. for healthy guinea pigs. In no case was a cure obtained.

Sazerac and Levaditi (1922) experimented on the curative action of bismuth in trypanosomiasis and state that positive results have been obtained. The same investigators carried out many experiments with rabbit syphilis with favorable results.

Robert and Sauton (1916) found that bismuth checked the growth of tuberculosis bacilli and that the salt exercises a bactericidal action on Spirocheta gallinarum and that there was a positive action on trypanosome infections in the guinea pig.

TOXICOLOGY

Higgins (1916), quoting from Steinfeld and Meyer, states that two forms of intoxication can be produced. "The manifestations in the first or acute class were convulsions, dyspnea and bradycardia, with a fatal termination. In the second or chronic type, the animals showed marked lassitude, ulcerative stomatitis, anorexia, diarrhea, loss of weight and body heat, albuminuria, and sometimes tetanic contractions. The postmortem examinations in the latter class revealed ulceration and necrosis of the mucous membrane of the colon. Their explanation of this condition was that the bismuth circulating in the blood in a soluble form was precipitated by the hydrogen sulphide in the colon, and that the newly formed bismuth sulphide produced a necrosis by blocking the capillaries and lymph channels.

"Dalche's conclusions were that the most striking feature of bismuth poisoning is the stomatitis. It is characterized by lesions of a brownish purplish color appearing on the tongue, buccal membrane and throat. It may remain stationary, but in the advanced cases the teeth are loosened, the gums become spongy, and there is a mild salivation. The breath has a fetid odor, and there is difficulty in swallowing. The lesion usually begins at the level of the molars and is most severe where the teeth come in contact with the mucous membrane. Generally these spots are covered by a whitish diphtheritic membrane surrounded by a blackish areola. Dalche believes that the stomatitis results from the elimination of the salt through the salivary glands, and may follow within a few days after the bismuth injection.

"Although most observers state that bismuth is absorbed from granulating surface only after it has been converted into an albuminate, Mayer and Baehr, after demonstrating the metallic granules within the leucocytes, are disposed to believe that absorption is largely carried on by phagocytosis. These heavily laden cells were found in the muscular tissue at a considerable distance from the portal of entry. According to these writers, the excretion of bismuth is mainly through the kidneys and the gastrointestinal tract, although others have demonstrated it in the bile, milk and saliva. The weight of evidence indicates that metallic bismuth poisoning results generally from the *local* application, whereas the toxic effects following the internal administration of the subnitrate salt result as a rule from the formation and absorption of nitrites.

"Bismuth, therefore, is not the innocuous drug once described, but to some individuals may prove to be most dangerous. *Sixty-five cases of poisoning with twenty-four fatalities should serve as a warning against its indiscriminate use.* Even Beck admits that of the 1,100 cases treated by him, 30 per cent showed pigmentation of the gums, thus indicating the absorption of the bismuth and its potentially toxic effects. We as medical men cannot refrain from noting with apprehension the unmistakable action of this agent on the kidneys and other organs in susceptible individuals."

Aubry (1922) showed that bismuth was detected in the urine even in dilutions of 1:600,000 of Bi_2O_3.

Day (1922) in studying the effects of bismuth on the kidneys states that the most striking result was a copious diuresis unaccompanied by strangury or other signs of vesical irritation. Nausea, stomatitis, and diarrhea were other symptoms of intoxication noted.

From this series of papers it has been observed that the toxicity of bismuth intravenously is much higher than intramuscular injections, and that the variation is considerable with various species of animals.

EXPERIMENTAL

In order to study these great discrepancies reported in the foreign literature, and especially to gain information about the salt and its action on protozoa, a careful application of American methods was utilized both for toxicity and trypanocidal activity.

The work in this laboratory has been conducted along the line of reproducing the soluble tartrobismuthates, all which crystallize as alkaline salts. These salts show an alkaline reaction to phenolphthalein when dissolved in water. Luatol which has been used for comparison purposes is used both in aqueous and oily suspension. The commercial sample of Trepol is obtained only in oily suspension and represents the insoluble type of product which can readily be prepared. Bismuthogenol is likewise an oily suspension containing a product which is insoluble in water with neutral reaction. Quantitative chemical analyses of these products showed considerable variation from the figures given to these products.

The oily suspensions were extracted with ether and the remaining solid analyzed for bismuth, determined as Bi_2O_3. The method will be described in a later article. These results were checked by another laboratory using the sulphide method. Three methods of preparation were employed, yielding water soluble products whose bismuth content was 16.80 per cent, 23.2 per cent, and 27.0 per cent. The confirming analyses gave 26.6 per cent bismuth. The study of the insoluble preparations is incomplete at the present time and no results are given on this type of preparation. Product M_4 is prepared practically the same as the description of Calcagno. The analyses were made by Mr. Levy of the analytical department of this laboratory.

THE TOXICOLOGICAL TESTING OF SODIUM POTASSIUM TARTROBISMUTHATE

New chemical compounds synthesized for the use of the physician in the treatment and eradication of protozoal disease should be tested for their toxicity and parasiticidal value insofar as can be done in the biological laboratory. The widespread use of organic arsenic compounds has resulted in the development and perfection of the animal tests needed for the proper control of these products. The purpose of the present work has been to apply, insofar as practicable, the methods of testing in use for arsenicals, to the testing of the compounds of bismuth. From the results obtained it is proposed to determine whether the same methods may be used in evaluating these compounds and to what extent the laboratory tests may be used as a basis for predicting clinical results.

The Test for Toxicity.—This test has been described in the Regulations (1920) issued by the U. S. Public Health Service. Healthy, white rats are bought at a weight of from 50 to 80 grams. They are kept in the laboratory on a standardized and complete diet. About one week to ten days before use, they are starved for 18 to 20 hours and then marked and weighed. Food is again removed the evening before the day of injection. This second weight gives the data required for the calculation of the rate of growth over the period of observation.

Voegtlin and Myers (1918, p. 848) as well as other writers have shown the importance of mineral constituents in the dietary of laboratory animals. With these experiments in mind as well as the work of Forbes and Keith (1914), the salt mixture (C.N.M. mixture) as given in the above mentioned article of Voegtlin and Myers was incorporated in the diet. The animals gained as much as 3 per cent of their body weight per day. However, most of the rats used in the present experiments on bismuthates were fed on the diet recommended by Dr. G. C. Lake of the Hygienic Laboratory, since it also seemed to contain sufficient mineral constituents, and by actual comparison similar gains in weight were obtained. The diet suggested by Lake is as follows: whole wheat (ground) 53.5 per cent, whole corn (ground) 10 per cent, skim milk powder 33 per cent, calcium carbonate 0.5 per cent, sodium chloride 1 per cent, and codliver oil 2 per cent.

The solutions for intravenous injection were made in sterile, freshly distilled water. Two hundred milligrams in 20 c.c. (1 per cent solution) made sufficient material for the injection of one lot of rats. Most of the solutions were allowed to stand fifteen minutes before the injection of the first rat, although it is quite probable that equilibrium is reached much before the end of this period. Injections were made into the saphenous vein, at the rate of 1 c.c. in 2 minutes, without anesthesia. Calibrated 1 c.c. syringes were used. Preliminary experiments on used rats gave an idea of the probable range of toxicity. When fresh rats were used, the doses were spaced at regular intervals of 20 per cent commencing with 30 mg. per kg. as shown in the tables on toxicity.

The animals were observed at least seven days after injection.

Autopsies were made on all animals which died. The surviving animals on the later tests were killed and autopsied. Some of the preparations examined were in the form of olive oil suspensions of the dry salt. These are designed for intramuscular use and were so injected in rats in order to determine their toxicity. Injections were made into the muscles of one or both hind legs of the rats. Those rats which survived were used in qualitative tests for trypanocidal activity with no further injection of the drug with the intention of discovering the effect of the drug on organisms after a period of one week. The regular test was carried out in the usual manner.

TABLE I

SODIUM POTASSIUM TARTROBISMUTHATE, "LUATOL" INTRAVENOUS INJECTION

DOSAGE. 30 MG. PER KG.

RAT NO.	SEX	% GAIN PER DAY	AGE OF SOL. MIN.	LENGTH OF LIFE	RESULT * DIED – LIVED
6666	F	0.63	9	7 days	*
6670	F	1.00	23	7 days	–
6673	F	1.00	32	7 days	–
6951	M	1.30	10	7 days	–
6954	M	2.15	19	7 days	–
6957	M	1.31	27	7 days	–

83.3% of the rats survived

DOSAGE 36 MG. PER KG.

RAT NO.	SEX	% GAIN PER DAY	AGE OF SOL. MIN.	LENGTH OF LIFE	RESULT * DIED – LIVED
6667	F	2.05	13	3 days	*
6671	F	0.67	26	7 days	–
6674	F	0.90	36	7 days	–
6952	M	2.18	12	7 days	–
6955	M	1.54	21	7 days	–
6958	M	0.33	29	5 days	*
7200	M	1.81	9	7 days	–
7204	M	2.29	19	7 days	–

75.0% of the rats survived.

DOSAGE 43 MG. PER KG.

RAT NO.	SEX	% GAIN PER DAY	AGE OF SOL. MIN.	LENGTH OF LIFE	RESULT * DIED – LIVED
6668	F	1.18	16	2 days	*
6672	F	0.69	29	4 days	*
6675	F	0.62	40	3 days	*
6953	M	1.04	16	7 days	–
6956	M	0.53	24	2 days	*
6959	M	0.98	33	3 days	*
7201	M	1.89	11	7 days	–
7203	M	1.20	17	7 days	–

37.5% of the rats survived

DOSAGE 51 MG. PER KG.

RAT NO.	SEX	% GAIN PER DAY	AGE OF SOL. MIN.	LENGTH OF LIFE	RESULT * DIED – LIVED
6669	F	0.86	21	Less than 24 hr.	*
7202	M	2.09	15	7 days	–

50.0% of the rats survived.

Table 1 shows the toxicological action of the water soluble tartrobismuthate of sodium and potassium when it is administered intravenously. The sex and the percentage gain in weight per day are important factors when the critical M. T. D. is approached. The survival of 60 per cent of the rats is required. Thirty-six mg. per kg. is the dose which is selected as the M. T. D. on this basis.

EXPERIMENTAL RESULTS

The macroscopic, pathologic findings in the animals dying from the drug included lesions of the kidneys, liver, and lungs in the order named. In addition to the hemorrhagic areas in the lungs a large amount of fluid was occasionally found in the pleural cavity. The most common lesion seemed to be that of the kidney. In

TABLE II

SODIUM POTASSIUM TARTROBISMUTHATE C. N. M. No. 1
INTRAVENOUS INJECTION

DOSAGE 30 MG. PER KG.

RAT NO.	SEX	% GAIN PER DAY	AGE OF SOL. MIN.	LENGTH OF LIFE	RESULT * DIED – LIVED
6960	M	1.21	14	7 days	–
6964	M	1.96	25	7 days	–
6968	M	1.52	37	7 days	–

100 % survivals.

DOSAGE 36 MG. PER KG.

RAT NO.	SEX	% GAIN PER DAY	AGE OF SOL. MIN.	LENGTH OF LIFE	RESULT * DIED – LIVED
6961	M	2.01	17	7 days	–
6965	M	2.13	28	7 days	–
6969	M	1.25	40	7 days	–

100 % survivals.

DOSAGE 43 MG. PER KG.

RAT NO.	SEX	% GAIN PER DAY	AGE OF SOL. MIN.	LENGTH OF LIFE	RESULT * DIED – LIVED
6962	M	1.78	20	8 days	–
6966	M	1.61	31	8 days	–
6970	M	1.95	43	8 days	–
7032	M	2.74	12	7 days	Killed
7034	M	2.72	18	7 days	Killed
7036	M	1.63	25	7 days	Killed
7124	M	2.98	30	7 days	Killed
7125	M	3.70	15	7 days	Killed

100 % survivals.

DOSAGE 51 MG. PER KG.

RAT NO.	SEX	% GAIN PER DAY	AGE OF SOL. MIN.	LENGTH OF LIFE	RESULT * DIED – LIVED
6302	M	3.16	18	4 days	*
6305	M	3.04	28	4 days	*
6308	M	3.13	37	7 days	–
6963	M	2.32	23	7 days	–
6967	M	1.29	34	7 days	–
6971	M	1.73	45	7 days	–
7033	M	3.36	15	7 days	Killed
7035	M	2.32	21	7 days	Killed
7037	M	3.17	28	7 days	Killed
7071	M	1.07	12	3 days	*
7074	M	0.97	24	3 days	*
7121	M	2.66	19	7 days	Killed
7122	M	2.79	22	7 days	Killed
7144	M	3.26	14	7 days	Killed
7147	M	3.60	24	7 days	Killed
7185	M	1.29	16	7 days	Killed
7189	M	1.82	28	7 days	Killed

76 % of the rats survived.

DOSAGE 61 MG. PER KG.

RAT NO.	SEX	% GAIN PER DAY	AGE OF SOL. MIN.	LENGTH OF LIFE	RESULT * DIED – LIVED
6249	F	1.48	17	5 days	*
6250	F	1.54	18	4 days	*
6251	F	2.46	21	52 hr.	*
6303	M	2.35	21	4 days	*
6306	F	0.65	31	3 days	*
6309	M	2.36	40	26 hr.	*
7072	M	1.06	16	3 days	*
7075	M	1.03	29	3 days	*
7123	M	2.37	26	7 days	Killed
7126	M	3.21	32	7 days	Killed
7145	M	2.69	17	7 days	Killed
7148	M	4.88	26	7 days	Killed
7186	M	1.55	19	7 days	Killed
7188	M	1.43	26	Less than 18 hr.	*

35.7 % of the rats survived.

DOSAGE 73 MG. PER KG.

RAT NO.	SEX	% GAIN PER DAY	AGE OF SOL. MIN.	LENGTH OF LIFE	RESULT * DIED – LIVED
6252	F	1.80	23	<44 hr.	*
6253	F	2.38	26	<44 hr.	*
6254	F	1.97	28	3 days	*
7073	M	0.71	19	2 days	*
7076	M	1.13	33	3 days	*
7146	M	3.47	20	3 days	*
7149	M	3.78	29	<24 hr.	*
7187	M	1.97	23	Less than 18 hr.	*

None of the rats survived.

The M. T. D. is 51 mg. per kg. It is observed that as the critical dose is approached, death occurs early after the injection (2 to 4 days).

those animals which were killed after seven days where lesions were found they were usually confined to the kidney and consisted of enlargement and necrosis of that organ.

From Table V it will be seen that, for the rat, the maximum tolerated dose per kilogram body weight (i.e., that dose which

TABLE III

SODIUM POTASSIUM TARTROBISMUTHATE C. N. M. No. 3
INTRAVENOUS INJECTION

DOSAGE 30 MG. PER KG.

RAT NO.	SEX	% GAIN PER DAY	AGE OF SOL. MIN.	LENGTH OF LIFE	RESULT * DIED – LIVED
6615	M	2.38	19	8 days	–
6618	M	2.01	29	8 days	–
6621	M	3.04	38	8 days	–
6942	M	1.60	11	7 days	–
6945	M	0.53	20	7 days	–
6948	M	2.26	29	7 days	–

100 % survivals.

DOSAGE 61 MG. PER KG.

RAT NO.	SEX	% GAIN PER DAY	AGE OF SOL. MIN.	LENGTH OF LIFE	RESULT * DIED – LIVED
7140	M	2.17	21	24 hr.	*
7141	M	2.49	24	4 days	*

None of the rats survived.

DOSAGE 36 MG. PER KG.

RAT NO.	SEX	% GAIN PER DAY	AGE OF SOL. MIN.	LENGTH OF LIFE	RESULT * DIED – LIVED
6616	M	1.30	22	8 days	–
6619	M	2.02	32	Less than 45 hr.	*
6622	M	3.17	41	Less than 21 hr.	*
6943	M	0.39	14	7 days	–
6946	M	1.09	23	7 days	–
6949	M	2.08	31	7 days	–
7180	M	1.03	14	2 days	*
7184	M	3.02	26	7 days	Killed
7195	M	2.46	14	7 days	–
7196	M	2.26	17	7 days	–
7198	M	2.59	22	7 days	–

72.7% of the rats survived.

DOSAGE 43 MG. PER KG.

RAT NO.	SEX	% GAIN PER DAY	AGE OF SOL. MIN.	LENGTH OF LIFE	RESULT * DIED – LIVED
6617	M	2.29	25	45 hr.	*
6620	M	3.40	35	21 hr.	*
6623	M	2.54	44	21 hr.	*
6944	M	1.50	17	7 days	–
6947	M	2.04	26	7 days	–
6950	M	2.47	35	7 days	–
6987	M	2.39	10	7 days	–
6989	M	2.29	16	7 days	–
6991	M	3.11	22	7 days	–
7138	M	1.81	15	7 days	–
7143	M	2.00	31	3 days	*
7181	M	1.83	16	3 days	*
7183	M	2.61	22	7 days	–
7197	M	2.50	19	2 days	*
7199	M	2.06	25	7 days	–

60% of the rats survived.

DOSAGE 51 MG. PER KG.

RAT NO.	SEX	% GAIN PER DAY	AGE OF SOL. MIN.	LENGTH OF LIFE	RESULT * DIED – LIVED
6988	M	1.82	13	2 days	*
6990	M	3.63	18	7 days	–
6992	M	1.90	25	2 days	*
7139	M	3.30	18	2 days	*
7142	M	2.22	27	2 days	*
7182	M	1.89	18	2 days	*

16.7% of the rats survived.

Table III shows the toxicological findings of preparation (C. N. M.) No. 3, designed to compare the relation of method of preparation and toxicity. The M. T. D. of this preparation is 43 mg. per Kg.

permits survival of 60 per cent of the animals) is as follows: for preparation No. 1, 51 mg.; for preparation No. 3, 43 mg.; for preparation No. 4, 51 mg.; and for preparation "Luatol," 36 mg. However, the tables on each dose must be considered with regard for the condition of the animals. When this is done it will be seen that these figures will, in some instances, bear slight revision.

Careful study of these tables indicates that rats showing a low percentage gain in weight per day are not likely to survive at the critical M.T.D. In other words the dietary factors involved in the production of the rat are nearly as important as the toxicity of the drug. Rats receiving large doses of the drug showed loss

TABLE IV

SODIUM POTASSIUM TARTROBISMUTHATE C. N. M. No. 4
INTRAVENOUS INJECTION

DOSAGE 36 MG. PER KG.

RAT NO.	SEX	% GAIN PER DAY	AGE OF SOL. MIN.	LENGTH OF LIFE	RESULT * DIED – LIVED
7002	M	2.0	15	8 days	Killed
7005	M	1.8	23	8 days	Killed
7008	M	1.1	33	8 days	Killed

100% survivals.

DOSAGE 73 MG. PER KG.

RAT NO.	SEX	% GAIN PER DAY	AGE OF SOL. MIN.	LENGTH OF LIFE	RESULT * DIED – LIVED
7084	M	1.8	15	Less than 24 hr.	*
7087	M	2.7	26	Less than 24 hr.	*
7192	M	2.1	22	Less than 18 hr.	*

None of the rats survived.

DOSAGE 43 MG. PER KG.

RAT NO.	SEX	% GAIN PER DAY	AGE OF SOL. MIN.	LENGTH OF LIFE	RESULT * DIED – LIVED
7003	M	2.2	18	8 days	Killed
7006	M	1.9	26	8 days	Killed
7009	M	1.7	37	8 days	Killed
7127	M	2.2	10	7 days	Killed
7130	M	3.1	21	7 days	Killed

100% survivals.

DOSAGE 51 MG. PER KG.

RAT NO.	SEX	% GAIN PER DAY	AGE OF SOL. MIN.	LENGTH OF LIFE	RESULT * DIED – LIVED
7004	M	1.8	20	8 days	Killed
7007	M	1.5	29	8 days	Killed
7010	M	1.9	40	8 days	Killed
7082	M	1.5	8	2 days	*
7085	M	2.0	19	7 days	Killed
7128	M	2.9	13	7 days	Killed
7131	M	3.5	23	2 days	*
7190	M	2.4	15	7 days	Killed
7194	M	2.3	30	2 days	*

66.7% of the rats survived.

DOSAGE 61 MG. PER KG.

RAT NO.	SEX	% GAIN PER DAY	AGE OF SOL. MIN.	LENGTH OF LIFE	RESULT * DIED – LIVED
7083	M	1.8	11	2nd day	*
7086	M	2.0	23	Less than 24 hr.	*
7129	M	3.3	17	7 days	Killed
7132	M	2.6	26	2 days	*
7191	M	1.8	18	18 hr	*
7193	M	2.6	26	18 hr.	*

16.7% of the rats survived.

Table IV shows the comparison of another sample prepared by a different method. The M. T. D. is 51 mg. per kg. Again early death is noted (2 days). The entire series of rats in this group showed an average percentage gain in weight per day of 2.2 per cent.

of weight indicating that much care should be exercised in the selection of a dose in clinical application. The tables show the dietary condition of the individual animals and length of life. All animals were autopsied so that a gross idea of the tissue changes might be observed. It may be observed that all of the preparations, when studied intravenously, show an M.T.D. of approximately 50 mg. per kg., indicating that this is a drug which should not be treated in a trifling manner.

THE ACTION OF SODIUM POTASSIUM TARTROBISMUTHATE ON EXPERIMENTAL TRYPANOSOMIASIS IN RATS

Since the time of Ehrlich and Hata the therapeutic value of organic arsenical compounds has been tested by determining their

TABLE V

SUMMARY OF TOXICITY TESTS ON TARTROBISMUTHATE PREPARATIONS. INTRAVENOUS INJECTION OF A 1 PER CENT AQUEOUS SOLUTION MG. PER KG.

PRODUCT	30 MG.		36 MG		43 MG.		51 MG.		61 MG.		73 MG.	
	NO. RATS INJEC.	PERC. SURV.	INJ.	SUR.	INJ.	SUR.	INJ.	SUR.	INJ.	SUR.	INJ.	SUR.
Sodium Tartrobismuthate No. 1	3	100	3	100	8	100	17	76.6	14	35.7	8	0
Sodium Potassium Tartrobismuthate No. 3	6	100	11	72.7	15	60	6	16.6	2	0		
Sodium Potassium Tartrobismuthate No. 4			3	100	5	100	9	66.7	6	16.7	3	0
Sodium Potassium Tartrobismuthate "Luatol"	6	83.3	8	75	8	37.5	2	50				

power to destroy living protozoa in animals. Investigators sometimes have used white mice for this purpose. However, white rats infected with the Trypanosoma equiperdum are used at present in order to make these comparisons. Recent work of Dale (1922) correlating the clinical and trypanocidal action of neosalvarsan has confirmed the statements of earlier writers that this method may be used as a measure of the value of arsenicals in the treatment of syphilis.

For the past few years this method with a few modifications has been employed by this laboratory in the study of the therapeutic activity of salvarsan and its derivatives. The application of this test to the evaluation of sodium potassium tartrobismuthate was made with the results as given in detail in the tables. It must be borne in mind that there are valuable, antisyphilitic compounds which seem to have little trypanocidal action. It is possible that the bismuthates fall in this class. If so, it will be necessary to test them on animals infected with Treponema pallida or some other organism more susceptible to bismuth.

On the other hand, bismuth alone may be valueless in the treatment of protozoal diseases and the remarkable clinical results may be explained by the synergistic action of arsenic present from the previous treatment with salvarsan or its derivatives. The results of experiments in these laboratories indicate that the presence of a subeffective dose of arsenic gives to the bismuthate a trypanocidal action that is not apparent with that element alone.

In general the method of testing is that used by Voegtlin and Smith (1920, p. 453) with such modifications as experience here has shown to increase the value of the test and the ease of executing it. The *principal modification involves the use of a standard drug,* preferably *salvarsan, as a control of the variables of the test.* The grade of the infection is believed to be a variable dependent upon the number of organisms with which the test rat is infected as well as the stage of infection of the seed rat. *The use of a control drug permits the treatment of animals* at any convenient time regardless of the number of organisms per cu. mm. provided, of course, that all the animals on a given test have approximately the same number of organisms. Tests have shown that the ratio of minimal effective dose (M.E.D.) of standard to M.E.D. of unknown is the same whether the infection be 20,000 or 200,000, although the actual number of milligrams per kilogram of drug required to reduce the infection is different.

The method of Voegtlin is further modified in that all rats are starved for 12 to 18 hours before treatment. This allows treatment at a predetermined time, whereas, if one waited for the infection to reach a given minimum, the animals would have to be starved over varying periods. The reason for starving the rats is that all doses are calculated on the basis of actual animal weight.

With the use of a control drug it is believed that two rats per dose are sufficient at intervals of 30 to 40 per cent. However, three rats per dose at intervals of 33⅓ per cent may be used and that dose be considered the M.E.D. upon which two out of three rats give a negative result within the time specified. It is believed that five rats per dose are not necessary with the use of a control drug.

Some of the work in the past has been done without counting of the organisms in the blood at the end of twenty-four hours. It is believed that less work is involved by the use of Dale's (1922) method which is similar to the one used here for the past few years, namely, daily observation for three days, recording as negative those specimens in which no organisms appear in at least ten fields. It has been found that those animals showing—(i.e., less than 1,000 per cu.mm.) will practically always become negative either on the second, third, or fourth day, and will usually remain negative for several days. However, in order to correlate the two methods of interpretation, counts have been made on such rats as were considered to have their infection reduced materially and the results have been recorded.

The technic of inoculation of rats involves the intraperitoneal injection of the organisms. The method of treatment is that of injection of the solution into the saphenous vein. Calibrated one c.c. syringes are used.

All solutions are made up with sterile freshly redistilled water in 50 c.c. graduated, glass-stoppered cylinders. The strength of the solutions is such as to allow an injection of 0.3 c.c. to 0.8 c.c. The calculation of the amount to be injected is facilitated by the use of the following equation:

$$\text{Amount to be injected in c.c.} = \frac{\text{Weight of rat in gm.} \times \text{dose is mg./kg.}}{\text{mg. per c.c. of solution} \times 1{,}000.}$$

The order of injection is that of rotation of both the products and the dosage, e.g., A, 1; B, 1; C, 1 . . . . ; A, 2; B, 2; C, 2; etc.

The rats used are healthy, normal rats of the same source and weight as those used on toxicity work. The diet used is the same, namely, that recommended by Dr. G. C. Lake of the Hygienic Laboratory of the U. S. Public Health Service.

The determination of the M.E.D. of a drug rather than the curative dose is favored for the reasons advanced by Voegtlin and Smith (1921). It is recognized that this is an indirect method of measuring the relative curative value of different compounds. It has the value of allowing a large number of tests to be conducted with but the time and space that are required to determine the curative dose. The old ratio of "dosis curativa" to "dosis tolerata" is replaced by Voegtlin and Smith, (1921, p. 374), with an "empirical therapeutic ratio" $\frac{\text{M.L.D.}}{\text{M.E.D.}}$. With healthy, normal, white rats on a standardized diet the M.L.D. should be constant. It is suggested that the new definition of M.E.D. be the number of mg. per kg. as shall cause disappearance of organisms from the blood stream at some time within three days after treatment of such an infection as will give an M.E.D. of X mg. per kg. with the standard drug. The value X should be determined by some laboratory such as the Hygienic Laboratory, Washington, D. C.

Observations of the animals at later periods than 24 hours have apparently been made by Voegtlin and his coworkers as will be seen by noting the definitions of the M.E.D. that have been given: Voegtlin and Smith (1920, p. 471), "Therefore, in this and later work, the term minimum effective dose means *the minimum dose which given intravenously will reduce the trypanosomes to none or a very few,* regardless of the time necessary to effect this reduction." Voegtlin and Smith (1921, p. 358), *"The minimum effective dose has been defined as that dose which will just clear the blood stream of parasites in twenty-four hours."* Voegtlin and Miller (1922, p. 1627), "The minimum effective dose is the dose required to bring the parasitic count within 24 hours to a trace or negative, or in other words, the dose which kills from 100,000 to 250,000 parasites per cu.mm. of blood. As a rule, the blood is again examined at the end of 48 and 72 hours after treatment." The use of a control drug and observations without counting over a period of three days after treatment appears to be an essential factor in establishing a reliable test. It is possible that on a given drug this may raise the M.E.D. 30 to 40 per cent but will not change the relative values of its and the standard drug.

It is our experience that at the M.E.D., and often in 30 to 60 per cent larger doses the maximum reducing effect is exerted at 48 or 72 hours. This is particularly evident in those rats showing from 250 to 1500 organisms per cu.mm. at the end of 24 hours after treatment and weighing 100 to 120 gm.

The test for trypanocidal activity as outlined above has been applied in the study of the bismuth compounds. The tables numbered VI to X give the results obtained. It will be noted that on infections such as are used in the testing of arsenicals there is no trypanocidal action until the minimum lethal dose is approached. Even here the action is so slight as to be of no value in obtaining a minimum effective dose as is done with the arsenic compounds. (See Table VI.) The result of decreasing the numbers of organisms is shown in Table V.

The infection of trypanosomes was intentionally lowered in order to ascertain whether the bismuthate was trypanocidal toward infections less than 100,000 to 250,000 per cu.mm. Results given in

TABLE VI

SUMMARY OF TESTS FOR TRYPANOCIDAL ACTIVITY OF SALVARSAN USED AS CONTROL IN ALL TESTS

DATE	INFECTION	WEIGHT LIMITS OF RATS, GMS.	M. E. D. MG/KG
8-17-22	133,000-228,000	89-122	4.9
8-29-22	104,000-304,000	95-139	4.5
9-12-22	61,000-197,000	114-144	4.5
9-14-22	84,000-318,000	121-152	4.5
9-19-22	31,000-83,000	108-150	3.4
9-21-22	110,000-166,000	120-158	4.5
9-26-22	5,500-21,000	136-159	1.9
10- 3-22	4,000-49,000	132-162	3.4

TABLE VII

TEST FOR TRYPANOCIDAL ACTIVITY OF "LUATOL."

INFECTION PER CU. MM.	DOSAGE LUATOL	RESULT 24 HR.	TREATMENT WITH NEO MG/KG.	FINAL RESULT
15,000	5.6	+++ (338,000	–	Dead under 48 hr.
14,000	5.6	+++ per cu. mm.)	5	Dead under 48 hr.
20,000	7.5	+++	–	Dead under 48 hr.
17,000	7.5	+++	5	Dead 48 hr.
11,500	10.0	+++	–	Dead under 48 hr.
16,000	10.0	+++	5	Dead under 48 hr.
7,000	13.5	+++	–	Dead under 48 hr.
17,000	13.5	+++	5	Dead under 48 hr.
15,000	18.0	+++	–	Dead under 48 hr.
8,000	18.0	+++	5	++++ Dead 48 hr.
116,000	22.5	Dead under 24 hr.		
11,000	24.0	+++	–	Dead under 48 hr.
19,000	24.0	+++	5	++ 48 hr. Dead<96 hr.
11,000	32.0	+++	–	Dead under 48 hr.
22,000	32.0	+++	5	53,000; ++ Dead under 96 hr.
72,000	34.0	++++ at 24 hr.		

TABLE VIII

TEST FOR TRYPANOCIDAL ACTIVITY OF CERTAIN BISMUTH COMPOUNDS C. N. M. No. 1

INFECTION PER CU. MM.	DOSAGE MG./KG.	RESULT
214,000	10.1	Dead under 24 hr.
104,000	13.5	Dead 24 hr.
100,000	18.0	Dead 24 hr.
92,000	24.0	Dead under 24 hr.
169,000	37.0	Dead
232,000		Dead
284,000	50.0	Dead
366,000		Dead
220,000	67.0	Dead
320,000		Dead

TABLE IX

TEST FOR TRYPANOCIDAL ACTIVITY OF CERTAIN BISMUTH COMPOUNDS
C.N.M. No. 3

INFECTION PER CU. MM	DOSAGE MG./KG.	RESULT
135,000	3.6	Died under 24 hr.
194,000		“ “ “
180,000	5.0	“ “ “
173,000		“ “ “
126,000	7.1	“ “ “
176,000		“ “ “
128,000	10.0	“ “ “
133,000		“ “ “
311,000	12.0	“ “ “
292,000	14.5	“ “ “
256,000	17.5	“ “ “
312,000	21.0	“ “ “
256,000	25.0	“ “ “
300,000	28.0	++++ Died
320,000		
330,000	30.00	Dead about 24 hr.
302,000	37.0	++++ Dead
274,000		
348,000	39.1	370,000 at 24 hr. Dead under 48 hr.
274,000	50.0	Dead under 48 hr.
468,000		“ “ “

TABLE X

TEST FOR TRYPANOCIDAL ACTIVITY OF CERTAIN BISMUTH COMPOUNDS
C.N.M. No. 4

INFECTION PER CU. MM	DOSAGE MG./KG.	RESULT 24 HR.	FINAL RESULT
250,000	37	Dead	
286,000		Dead	
326,000	50	++++ Died	
346,000		++++	Dead 48 hr.
354,000	67	Dead	
286,000		Dead	

this laboratory show it to have little trypanocidal action even with the lowered infection. It will be noted that the M.E.D. of salvarsan on this infection was 1.9 mg. per kg.

Voegtlin and Smith (1920, p. 492) have called attention to the complementary action of arsenic and antimony in experimental trypanosomiasis and Myers (U. S. Pat. 1,422,294, 1921) has invented and patented certain arsenostibino analogues of salvarsan and its derivatives. However, certain organic compounds of either metal alone have a marked trypanocidal action. The complementary action of bismuth and arsenic was accordingly tested in a preliminary experiment with the results shown in Table VII. All the rats on the tartrobismuthate alone died under forty-eight hours after treatment. This is the result that may be expected of rats receiving no treatment. Twenty-four hours after the bismuthate treatment one-half of the rats were treated intraperitoneally with a subeffective dose of neosalvarsan, 5 mg. per kg. Death was delayed in two of these rats forty-eight hours beyond the time of death of the corresponding rats that had no arsenic and which died on the day of death of all the other rats treated with bismuth. That the arsenic was given in insufficient amount to effect a measurable reduction is shown by the fate of the animals on doses of bismuthate lower than 24 mg. per kg.

It is proposed to study further the complementary effect on arsenic compounds of bismuth and other metals which alone are not trypanocidal.

Table VI shows a composite summary of the results obtained on the salvarsan control which was employed each time that the bismuth salts were tested. The low results for the M.E.D. were obtained on low infections. A uniform value was obtained on the high infections. When the bismuth preparations were compared, Tables VII to X, with the arsenical the results showed that there was little trypanocidal activity. In Table VII "Luatol" was tried on low infections and inasmuch as no activity was manifested, it was deemed unnecessary to use the high infections. Tables VIII, IX and X give the detail results of the American product in which high infections were used. No action was noted which indicates that the reducing dose is appreciably lower than the tolerated dose.

However, it should be stated that evidence is at hand that the presence of arsenicals is highly efficacious in causing the destruction of organisms with bismuth.

In a later paper the details of the intramuscular studies will be found. At this time it should be stated that there is a marked difference between the toxicity of the water soluble product and the insoluble drug. A warning in regard to the caseous residues after intramuscular injections should be sounded at this time. Local irritation and unabsorbed, oily cysts are noted together with emaciation. Like all subcutaneous and intramuscular injections the absorption is variable and hence the dosage is uncertain. Bismuth preparations examined in this laboratory have shown no trypanocidal activity either intravenously or intramuscularly, with the exception of a slight inhibition in larger intramuscular injections. Synergistic action of arsenic and bismuth shows some promise.

The intramuscular studies of the soluble and insoluble product are being continued and it may be possible that bismuth, on account of its acid and basic properties, will be an important addition to the antiluetic drugs. In comparison with the arsenicals, bismuth is inferior but in its relation to mercury it may find a place in syphilis therapy.

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THE SYPHILIS DEPARTMENT OF THE IN-PATIENT HOSPITAL: ITS PERSONNEL, ORGANIZATION, AND EQUIPMENT

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THE SYPHILIS DEPARTMENT OF THE IN-PATIENT HOSPITAL

ALTHOUGH special hospitals for syphilis may come into being, and may fill a long felt need, it has seemed that the general hospital requires facilities for syphilitic patients who would be better served by confinement to bed; for interesting cases worthy of study; and for patients with infectious lesions whose social life would make them a particular menace to the community, if at large.

PERSONNEL

The medical personnel of the syphilis section of the in-patient service should include a number of attending and assistant attending physicians. It would be best to have the physicians in attendance on the out-patient syphilis department fill these positions and in similar order of seniority, that is, there should be a director with complete charge of the service, and two attending physicians to serve under him. The junior men of the clinic staff would have ward duties of minor nature to those of the attendings, and substitute for them if need be. The chiefs of other services in the hospital, as medicine, surgery, gynecology, obstetrics, urology, pathology, serology, bacteriology, neurology, and psychiatry should be on the calling staff of the syphilis in-patient department, and subject to call for special examinations and advice.

The interne situation of this ward should be that each hospital interne have at least three to six months on the service of an 18 months' or 30 months' internship. If it is feasible to offer a residentship to one of the graduates, this should be done, and the period of service of such a resident should not be less than one year, preferably two years, after hospital graduation but not more than three years. The interne best adapted for promotion to resident should be selected.

There should be the greatest spirit of cooperation between the service of syphilis and the other services in the hospital. No tendency to harmful rivalry should be tolerated. The scope of the syphilis service should be made part of the record of both the lay and medical governing boards of the hospital. It should be definitely stated whether the ward service be limited to infectious, active, visible syphilitic lesions; whether the result of syphilitic involvement of the nervous tissue means admission to the syphilitic ward, or to a psychiatric service (where one exists); or whether syphilis is to be divided into systems and regions of the body so that heart syphilis goes to internal medicine; oral syphilis to its department, etc., etc. On the other hand, one should decide whether the syphilis department is to be made the dumping ground for every admission whose symptoms are obscure, yet whose Wassermann is positive, or even negative. This should not be encouraged, for then the syphilis service will be a dead weight on the rest of the hospital. Complete harmony between the men will alone show the way for carrying on the difficult duties of maintaining peace in the organization. Only with men of the highest caliber and professional attainment can one secure complete success.

DENTIST

There should be a staff dentist on duty with the syphilis department. One of the junior attending dentists to the hospital should be on duty certain hours during the day with equipment and instruments located on the ward for exclusive use therein. This dentist should be given the opportunity of making himself acquainted with every manifestation in or about the mouth which presents itself on the service. Rotation of the dentist may be practiced if more than one is available.

NURSING STAFF

Until the service for syphilitic patients has reached some proficiency and possibilities of poor technic have been abolished, I would recommend the employment of graduate nurses. With ease of operation, pupil nurses (if the hospital has a training school) may be assigned to these wards.

EMPLOYEES

The clerks, and stenographers employed in the ward should be mature persons and those having previous hospital experience should be given preference. Orderlies and scrub women should be informed of the possibility of contagion although it should not be necessary to give these people a postgraduate course of instruction in the disease. The cooks, dispensers, laboratory assistants, store keepers and others whose duties do not require attendance on the sick of this ward or handling any objects recently open to contamination from the ward need be no different or treated differently than others employed on other wards. Those whose duties, on the other hand, require attendance in the ward or manipulation of clothes, utensils, dishes, etc., which have recently come from the ward should be instructed similarly to the orderlies and scrub women.

THE WARD

Although a hospital or a pavilion made up entirely of individual rooms is ideal, the need for rigid economy of space and money has led to the development of the ward unit. It is essential to have the ward service for syphilis allotted space for itself, or it could be a unit connected by corridor to the rest of the hospital. In this communication, I would take a unit of 25 beds as the minimum for which a separate service for syphilis should be maintained. It would be feasible to divide this unit into two sections, one of 16 beds for male patients, and one of 9 beds for female patients. A large ward could be fitted to hold all the beds of its division except one or two for which provision could be made in a smaller room. The female small room could also contain a cot for any mother-baby patients. In addition to the ward space for beds, the unit would require space for ward kitchen, linen rooms, supply room, room for physicians, record room, photographic room, examination and treatment room, ward laboratory, nurses' rest room and wash room, room for students, x-ray, and dental room. The scullery should be fitted with live steam as should be the sterilizing room. A laundry system should be installed which requires no handling of soiled clothes. The use of the individual laundry bags by the patients with a carrier system and septic and aseptic laundry trails assures this. The use of washing machines with pressure tubs permits the use of the hospital laundry. Of course, in the enumeration of the rooms above, it is quite within reason to suppose that each one itemized need not be a separate and distinct physical compartment, if the space at the disposal of the syphilis department is curtailed. One room may serve a number of allied purposes, but many rooms named are distinctly necessary.

A number of other factors require brief mention, as for example, the installation of hot and cold water and live steam; foot pedals for all purposes including toilet flushing; proper heat units; ventilation; windows; artificial and natural lighting; walls (tiled to about 6 feet so as to be washable); vacuum cleaning; and facilities for disinfection and incineration. The toilet seats should be arranged as to permit the use of paper cover seats. Fixtures for paper towels should also be provided, and the required receptacles for used ones.

THE PATIENTS

The problem of what patient to admit to the ward service of syphilis is indeed a difficult one in the general hospital. Depending on the character of the hospital, part of this problem is settled by the rules and regulations governing the rest of the hospital. The city or free hospital would not have the problem of exacting payment from patients ill able to afford a hospital fee. On the other hand, once the patient is admitted to the hospital for any disease requiring treatment, the fact that he also requires antisyphilitic treatment should not be sufficient to alter the original assignment except with the consent of proper officials and the medical men of both services concerned. Where any difference of opinion comes up, the first service to which the patient had been assigned has the preference in any question regarding holding the patient, but if the service for syphilis is unwilling to accept the patient, the assigned service must either retain the patient, or discharge or transfer to some other institution for bed treatment, or to the out-patient syphilis clinic for ambulatory treatment. The need of such a provision is readily recognized and amounts to an anti-dumping order. Whether to admit syphilitic patients to the private side of the general hospital is another question which could only be answered by knowing the hospital, its general problems, and the way they are handled. Individuality would be required, as for example, what objection could there be to the admission of a syphilitic without lesions to the private side of the hospital for spinal puncture?

ADMISSION OF PATIENTS

The admitting officer of the hospital should be a salaried physician, and when feasible, one of the recent graduates could occupy this position. Every patient should be examined completely, and in particular for the infectious and contagious diseases, and parasites. The presence of other disease than syphilis should be sought in particular prior to admission to the ward for syphilitics. The garments worn to the hospital should be removed and hospital clothes provided.

Unless otherwise indicated all the clothes should be sterilized before they are stored or returned to the patient on discharge. The fastidious would require that money or other personal articles which the patient carries to the ward should also be sterilized. On being admitted to the ward, and after the diagnosis has been confirmed the senior ward physician may order that the patient receive a chart of information for patients, (see ''Syphilis Clinic'' *Boston Medical and Surgical Journal,* Dec. 9, 1920).

If the service for syphilis is admitting for a particular problem in which the staff is interested for the time, the names and addresses of other applicants for admission not suitable for immediate acceptance should be recorded for future use.

If an ambulance had been utilized for the transfer of a patient found to be suffering with infectious lesions, the ambulance accoutrements which may have been in direct contact with the open lesions, as blanket, stretcher, etc., should be removed and sterilized.

If the patient has been on the ward but his treatment is to be intermittent in character, he may be given a leave of absence or discharged for readmission when required. This tends to keep the case history compact rather than a series of copied short notes.

WARD HISTORY

Probably as important a task as any other on the ward for syphilis is that of keeping proper data on the patient as represented by the chart of his history, physical examination, pathologic reports, treatments, and course of the disease as manifested by changes in the eruption, clinical signs, and laboratory findings. One of the junior attending physicians should be assigned to chart rounds, and with the senior house physician should examine each chart at least once each week, and just previous to the discharge of the patient. Unless the chart is properly checked some points of vital interest to later investigation will be found lacking. The type of chart form to be used cannot be prepared at a moment's notice, and much care and attention to detail should be given so that as much information as possible be elicited from all patients in a more or less orderly fashion so that tabulations and résumés may be made at some future time. The use of an outline with blank spaces to be filled in with a word or a number cannot be entirely recommended, although admittedly of some benefit. It seems far better to prepare the chart, and have a list of leading questions printed on the bottom of the page to act as a reminder to the historian. In the beginning, the regular hospital chart could be utilized, or some such arrangement as given in my paper on the "Syphilis Clinic."

PATIENT ON THE WARD

Every patient admitted to the service whether from the outpatient department, or other source should have a history taken, correlated with clinic or other history, and recorded. Some of the common points of historic interest may be filled in on the outline provided for the purpose. Other individual facts should be recorded, and it should be distinctly understood that because no blank or space had been provided for any details the patient may disclose regarding the past or present symptoms, is not taken as an excuse for failure to record them on the history. A complete physical examination should be made, and the findings recorded. In any instance of doubt the consultant from the proper department is to be called for examination. Serological examinations, bacterial examinations, fluid examinations, etc., will be made on the ward if feasible, in the laboratory, or in the general laboratory of the hospital by the junior interne under the supervision of his senior or resident or the pathologist. On the ward service every effort should be made to have clinical syphilology the standard of diagnosis, but every means of physical examination, clinical pathology, and x-ray should be used.

Of course in the so-called latent syphilitic cases, history and confirmed serologic diagnosis in the form of highly positive Wassermann and substitute reactions should in the absence of other diseases known to give a positive (paradoxical) reaction be considered as evidence of syphilis and treatment instituted. The importance of syphilis to diseases of the internal organs, especially the cardiovascular and nervous systems, should be overemphasized rather than dismissed in the ward service for syphilis. The importance of the patient rather than his disease must be considered in these patients, and the mistake of overtreating syphilis because of its presence should not be made. Laboratory evidence alone of disease of the nervous system should not be accepted without confirmation of findings by clinical examination and neurologic tests, not only for the gross and readily evident changes but for the subtle variations which forecast mental and nervous disintegration. The bed service for syphilis should be the clearing house in this respect for many of our problems.

TREATMENT

The bed treatment of the bed patient with syphilis would depend entirely upon the indications presented by the individual. In the main, in otherwise healthy young persons, intensive courses of arsphenamine and mercury may be administered and in older persons larger doses than the ambulatory character of clinic practice permits may be administered. Patients with disease of the cardiac and vascular systems may also be treated with more certainty of results. Of course, spinal treatments are assured on a bed service, for although some clinics make a practice of diagnostic puncture, treatments should not be attempted in a clinic without bed facilities.

The details of treatment with the arsphenamines need be no different than that of treatment elsewhere. Mercury on the bed service should be the soluble group as the only advantage claimed for the insoluble group is that injection need be given but once in five days or once a week. With the patient at hand, injections of mercury every day could be given if the drug were indicated. Whether the patient should be treated in bed or in the treatment room will be decided on the character of the patient, and his known reactions to medication. Patients with visceral lesions would best be treated in their beds thus avoiding transfer to and from the treatment room. Of course, all precautions and preparations for the patient and the medication should be fulfilled.

A treatment cart could well be utilized and wheeled from bed to bed. With a little ingenuity and small expense such a cart could be improvised.

Many syphilitic patients on the bed service for syphilis would require attention from the physicians or other services of the hospital, and it should be given with a view to prophylaxis among those in the other wards. A woman with condylomata lata, about to be delivered of a child could possibly best be treated in the obstetrical department if she had been admitted too near term to receive antisyphilitic treatment. On the other hand, if any time at all were available, and no contraindications for antisyphilitic treatment existed, the ward service for syphilis would be the place for the patient until the hour of expected delivery. The patient with secondary syphilis and pneumonia would probably best be treated on the medical wards until the drop in temperature and the clearing of the pulmonic process permitted the assumption or resumption of antisyphilitic care. In practice, however, it will be found best to hold all infectious patients to the syphilis ward.

A patient treated on the wards of other services and who is also syphilitic should be transferred to the syphilitic department prior to the discharge of the patient for initial antisyphilitic treatment. The syphilis department could then make the effort to have the patient continue the antisyphilitic treatment. In this manner many patients would be properly instructed and in all likelihood continue treatment. This is an important duty for it acts as a prophylactic measure of no mean proportion.

One of the most difficult things on a service of this nature is to preserve the hospital attitude—that the patient is a sick person—and to avoid in every way possible any hint that syphilis and moral wrong doing are associated. The ward is for medical and sanitary purposes.

The regulations of the local board of health should be followed regarding the reporting of cases of venereal disease. It is very important that no case be reported in which any doubt of the diagnosis exists. If the regulations permit the use of initials or hospital number for reporting the cases this provision should be taken advantage of, and the name of the patient withheld.

WARD SUGGESTIONS

It is essential to keep a ward record of requests for consultation with the other departments, and the name of the patient with the department called should be entered, and not crossed off until the consultation has been held and the report rendered. Similarly, a list of Wassermanns and other laboratory work should be kept, and a check made on the receipt of the report and its entry on the patient's chart. An order book for the physician should be kept. A list should be made up each day of the patients to be treated the next day, and a separate list should be made for those to receive arsphenamine, mercury, etc. The arsphenamine list should also be considered as a supplemental diet list, and on the days of treatment, the diet should conform to the standing orders for the type of treatment to be administered.

Patients with lesions suspected of being primary lesions or other lesions which are to be studied for bacterial evidence of disease (spirochete examinations, dark-field stain, etc.; culture for Ducrey or Vincent's organisms) should not be permitted to apply any type of dressing with or without ointments or solutions except on direct written order of the house physician. It should be a routine procedure for the Wassermann, if negative, to be repeated once weekly for at least seven weeks unless positive, or unless the bacterial or clinical evidence is deemed worthy of sufficient weight to have treatment instituted prior to the termination of the seven week period or before the Wassermann becomes positive.

One of the most important considerations for patients, especially those with oral lesions and those undergoing treatment with mercury, is to have the proper hygiene of the mouth. Such patients are to be seen by the dentist and his recommendations for immediate work carried out. In addition every patient is to have an individual tooth brush, with instructions to use it night and morning.

In some hospitals, it may be necessary to keep patients who are under police supervision, as prisoners, persons held as material witnesses, etc., etc. The presence of a uniformed officer on the ward often introduces new difficulties but these must be met as best possible according to the situation of the service at the particular moment. Of course any patient of this character could not be discharged without notification of the proper police officials. Similar difficulties may be encountered in the case of paretics who may be admitted to the syphilis ward, who become violent or otherwise unmanageable.

The possibility of ward patients who are convalescent or otherwise fit being required or permitted to do light tasks on the ward or in the hospital should not be overlooked by the managers as it forms a means of keeping the interest of the patient alive, and unless contraindications exist, patients may be allotted some duties. Under certain circumstances, and with a particular class of patients, efforts of teaching useful arts or even the elements of rudimentary education may be made with profit.

The admitting officer or other physician noting the presence of active, infectious lesion on a patient of the syphilis ward, should order him placed on the precautions list, and the proper identifying tag or marker placed on the chart and over the foot of the bed.

On admission, the weight of the patient should be taken. Stripping of the patient or weighing with hospital slippers and bath robe may be chosen and the same procedure followed for all weights. The weight should be taken once each week after admission for all patients able to leave their beds.

The bathing of patients should be on order of the house physician. The use of the shower bath should be indicated for all patients with infections lesions; and the tub bath should be given only to patients free of cutaneous lesions. The tub and floor of the shower should be cleansed by the use of weak carbolic or lysol.

The use of rubber gloves in all manipulations should be made mandatory for the nurses when handling instruments, or the person of the patient. Precautions should be taken regarding the coughing of patients with infectious mouth lesions.

Thermometers should be individual for each bed, and after each use immersed in a solution of 1:1000 bichloride of mercury solution.

Temperatures to be taken by mouth twice daily unless otherwise ordered.

Rubber gloves, and instruments used on cases of active syphilis must be sterilized by boiling with plenty of water after each use.

Each patient should have his own tray, dishes and silverware plainly marked with the name or number of the bed. The dishes used should be sterilized after use, washed and returned to the proper patient.

The lavatory should be provided with paper seat covers. If the bed pan is used, it should be sterilized each time after use.

The exchange of newspapers and magazines by a number of patients should be discouraged. Books could be provided if to be kept by the patient.

Incoming mail need not be interfered with, but outgoing letters from patients with infectious lesions, should be retained for a period of 24 hours in a drier. By having envelopes supplied without gluing, the use of saliva for moistening is effectively prevented. Stamps could be affixed by machine or done in the office of the hospital after the drying period for the letter.

Visitors may be permitted, but no patient with infectious buccal lesions should be allowed visitors. No visitor should be allowed to see a screened patient without the permission of the ward physician, and only if a nurse or attendant is to be present.

Smoking should be prohibited.

Any dressing, bandage, cloth, or cotton which has come in contact with an open wound or surface of the patient is to be sterilized, if useful, or destroyed in the incinerator.

No patient may leave the hospital without permission of the medical and governing chiefs, but any patient who insists on leaving the hospital may do so on signing a release provided the local or other health regulations permit this.

SUPPLIES FOR SYPHILIS WARD SERVICE

The wards should be fitted with the ordinary drugs required in the nursing care of patients, and the special drugs as the arsphenamins, distilled water, fresh sodium hydroxide solutions, etc., may be ordered as required from the hospital pharmacy. Stationery should be provided for correspondence with especial features so that envelopes to be sent to patients do not reveal the source of sending. Certain supplies, as apparatus for administration of arsphenamin, are especial requisites for this ward, but otherwise the modern equipped ward is well able to handle syphilitic patients. In the ward laboratory one should provide complete dark field microscope in addition to the usual apparatus. A photographic equipment, or at least sufficient to take clinical photographs, is a great aid.

OTHER SUPPLIES

The other rooms and compartments of the syphilis ward need be little different from similar sections of other wards. The kitchen and pantry require a sterilizer for the returned dishes, and silver ware. In my opinion, the service should be individual, and each bed have a set for itself. If the beds were named or numbered, the name or number could be marked for all the supplies of each bed, and always returned to the bed. However, if the sterilization is always done, this refinement need not be met. The bath room for the patients should be fitted with shower baths. The dental equipment need be no different from dental units elsewhere. The facilities for sterilization should be adequate, and the dental instruments purchased with a view to their adaptibility for repeated sterilization. The chapter on prophylaxis of my paper on: ''Oral Syphilis,'' a consideration of this subject especially intended for dentists in the *Dental Cosmos* for May, 1920, may be consulted in this regard. The staff room, and the retiring room for nurses should be plentifully fitted with wash basins, and soap containers.

The x-ray department of the hospital may serve this ward as other wards. As a precaution, a patient should be permitted to leave the syphilis ward only if accompanied by a nurse or orderly, if sent to x-ray.

The pharmacy of the hospital will serve this department as the others.

A central laboratory may take charge of the more advanced work of clinical pathology, tissue work, colloidal gold reactions, Wassermann reactions, etc.

OBSERVATIONS ON KAHN PRECIPITATION REACTION FOR SYPHILIS

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IN previous papers[1] from this laboratory the writer described a simple precipitation test for syphilis based on the employment of syphilitic serum and alcoholic extract antigen of heart muscle with and without the addition of cholesterin. The utilization of tissue extracts in precipitation tests for syphilis has been discussed by Michealis,[2] Jacobstahl,[3] Bruck and Hidaka[4] and Hecht.[5] More practical precipitation tests have recently been proposed by Meinicke,[6] Sachs and Georgi,[7] Dreyer and Ward,[8] and Hecht,[9] the last being an outgrowth of Hecht's original method. Several other precipitation as well as turbidity tests have since been proposed by Dold,[10] Wang,[11] Bruck,[12] and Meinicke.[13] The extent to which the reaction under discussion differs from the above named reactions will be fully considered in forthcoming studies. In this paper several observations on the author's test based on experience gained with over 27,000 examinations made in this laboratory during the past year will be discussed.

I. THE PRECIPITATION TEST FOR SYPHILIS PROPOSED BY THE AUTHOR

Preparation of Antigen.—Beef hearts are freed from fat, fiber and blood vessels in the usual manner and passed several times through a meat grinder. The ground muscle is spread in a thin layer on a platter and dried at room temperature by placing in front of one or more revolving fans. The dried material is broken up into small pieces and passed several times through a coffee grinder, or ground in a mortar until very fine. A given quantity of this material (50 gm. or more) is placed in a 500 c.c. Erlenmeyer flask and sufficient ether added to make a layer of about 1 inch above the dried muscle. Extraction is permitted for about 24 hours at ice box temperature when the supernatant ether is poured off and replaced with fresh ether. This is repeated several times until supernatant ether is water clear. The ether is then filtered off and the heart muscle dried at room temperature (by spreading on a paper) until free from ether odor. The ether is discarded.

The dried material is extracted with absolute or 95 per cent alcohol in the proportion of 1 gm. to 5 c.c. A given quantity, such as 50 gm. of material, is placed in a 500 c.c. Erlenmeyer flask and 250 c.c. of alcohol added. The extraction is carried out for 9 days in the ice box and 1 day at room temperature. The alcoholic extract is filtered off and 0.4 per cent of cholesterin is added to a given amount. The cholesterin is dissolved by warming in the water-bath and shaking. The cholesterinized antigen is permitted to stand 24 hours before using. The noncholesterinized antigen may be used at once.

Dilution of the Antigens for the Tests.—1. One c.c. cholesterinized antigen is pipetted into a test tube having an inner diameter of about ⅜ inch or a 10 c.c. cylinder of about the same diameter.

2. Three c.c. salt solution (0.85 per cent) is measured into a 10 or 25 c.c. cylinder.

3. The saline is poured into the antigen tube with reasonable rapidity and the tube is immediately inverted back and forth.

4. The mixture will be opalescent and clear and is ready for use. Some mixtures show a marked tendency toward precipitation on standing, particularly in the cold. To overcome this tendency, the tube is placed in the incubator or in a glass of warm water until ready for use.

5. The noncholesterinized antigen is diluted in the same manner except that 2 c.c. of salt solution is added to 1 c.c. of antigen.

6. Different quantities (0.3, 0.5, 0.8, etc.) of the antigens may be diluted in the same manner provided 1 part of cholesterinized antigen + 3 parts of salt solution is employed and 1 part of noncholesterinized antigen + 2 parts of salt solution is used.

The Test Proper.—1. Measure two 0.3 c.c. quantities of clear inactivated (½ hour at 56° C.) serum into 2 small test tubes. Add 0.05 c.c. of the diluted cholesterinized antigen to one tube and the same amount of the noncholesterinized antigen to the other.

2. Shake rack vigorously about 2 minutes.

3. Observe spontaneous precipitations. If indefinite, examine tubes about half hour after incubation.

4. Place rack in incubator at 37.5° C. and observe next morning.

The Reading of Results.—1. Examine results without shaking the tubes. The typical precipitates are suspended in the medium. When reading weak positive reactions, slant the tube until it is almost horizontal; hold it about 10 inches above the eye level and observe the precipitate at the upper point of contact between fluid and inner tube wall.

2. The tests are read in accordance with the following scale:

I. Large clumps (one or more) = ++++.
II. A large floccular or granular precipitate = +++.
III. A moderate sized floccular or granular precipitate = ++.
IV. A fine floccular or granular precipitate = +.
V. A very fine floccular or granular precipitate = ±.

3. Old serums may show fine precipitates settled on the bottom of tubes after overnight incubation. These are nonspecific reactions and are considered negative. False precipitations can be avoided in many cases by clearing the serums by heavy centrifugation before using in the tests. Serums which show even slight contamination may give false one plus reactions.

4. The controls consist of three positive and three negative serums.

The Spontaneous Reaction.—After adding the antigen-salt solution mixture to the serum and shaking vigorously for several minutes, a distinct precipitate suspended in a clear medium will be observed in strongly positive serums. The typical precipitate will show a tendency to coalesce on standing so that if observed again in fifteen or thirty minutes, the particles will be found to be considerably larger. Old and particularly improperly centrifuged serums will occasionally show faint nonspecific precipitations. These never coalesce into larger particles and they settle on the bottom of the tube on standing.

The Micro-Procedure.—This is carried out with 0.03 c.c. of serum and 0.005 c.c. of antigen. Great care must be taken to see that the antigen is properly mixed with the serum. The tubes should be corked during the incubation period to prevent evaporation. The results approximate closely those obtained with regular quantities.

II. OBSERVATIONS ON AUTHOR'S PRECIPITATION TEST

The following discussion on the various phases of this test will be limited to the cholesterinized antigen test. The employment of a noncholesterinized antigen as a check on the cholesterinized one may prove of advantage in determining the effect of treatment, the former antigen becoming weaker or negative far more rapidly than the latter. In routine work, however, we prefer the employment of duplicate precipitation tests with two different cholesterinized antigens.

Remarks on Preparation of Antigen.—An antigen should preferably be prepared from more than one heart. As a general rule it may be stated that the more hearts employed in the preparation of a given antigen the better. Our experience is limited to beef and pig hearts. It is conceivable that an antigen prepared from human heart will be more sensitive. There are practical difficulties, however, to be encountered when attempting to obtain several human hearts at one time. And we are inclined to believe that a number of beef or pig hearts will produce a more uniform and possibly a superior antigen than a single human heart.

After the fat-free heart muscle is passed several times through a meat chopper, it is spread in a thin layer on a platter and dried by means of an electric fan. In the course of five to six hours the exposed surface will be quite dry, while the material underneath will be moist. The ground muscle is then turned over so that the moist part will be exposed to the fan, and allowed to remain overnight. By the next morning, dried plates will have been formed which are broken up into small pieces and drying continues for several hours.

The grinding of the dried material may be carried out with a mortar or with an ordinary coffee grinder which is used for no other purpose. The dried muscle need not be ground into a powder form. Good results will be obtained with material which is slightly gritty when rubbed with the fingers.

We have been accustomed to keep on hand a considerable amount of ground heart muscle and extract given quantities from time to time with ether and alcohol as antigen was needed. We have recently learned, however, that the keeping of dried heart muscle for any considerable period (even at ice box temperature) tends to reduce the sensitiveness of the final alcoholic extract. This may be due to autodigestion of the heart muscle. On the basis of this observation, we believe it best to extract the heart muscle with ether and subsequently with alcohol immediately after drying and grinding.

The ether and alcohol extractions of the ground muscle should be carried out in Erlenmeyer flasks. These should be approximately ten times as large as the quantity of material to be extracted. Thus 10 gm. of dried muscle should be extracted in 100 c.c. Erlenmeyer flasks; 25 gm. in 250 c.c. flasks and 50 gm. in 500 c.c. flasks. These requirements should be particularly adhered to in the case of alcoholic extractions to insure approximately uniform extracts.

The alcoholic extract should not contain an excessive amount of lipoids. The amount of lipoids contained in a given extract may be readily judged by the amount of coloring matter present. An extract rich in coloring matter is likely to be less sensitive than one containing a moderate amount of coloring matter. The probable explanation of this has been touched upon in a previous paper. An alcoholic solution containing 0.4 per cent cholesterin mixed with three times the amount of salt solution will precipitate the cholesterin. If, on the other hand, an alcoholic extract of heart muscle containing 0.4 per cent cholesterin is mixed with the same amount of salt solution an opalescent solution will result. The lipoids apparently are capable of keeping the cholesterin in solution. If a given cholesterinized antigen contains an amount of lipoids insufficient to keep the cholesterin in solution, a precipitate will be formed after mixing with salt solution, and render the mixture unfit for use. If, on the other hand, a given antigen contains an excessive amount of lipoids, the cholesterin is kept in solution in so stable a form (after mixing with salt solution) that the tendency to produce precipitation in the presence of positive serums may be considerably reduced.

Alcoholic extracts, on addition of salt solution, should produce mixtures which will be opalescent and clear and at the same time unstable. Extracts containing moderate amounts of lipoids will be found to conform with these requirements. Such extracts after being mixed with three parts of salt solution will be found to be opalescent and clear at incubator and, in many cases, at room temperature but will precipitate in the ice box. This tendency toward precipitation in the cold would indicate that we are dealing with an unstable mixture, and in our opinion, helps explain the marked tendency toward precipitation on mixing with positive serum.

In our last communication, we advised that the alcoholic extraction of the heart muscle is to be carried out for nine days in the ice box and one day at room temperature. This mode of extraction will be workable in most cases. Occasionally it will be found that with certain quantities of heart muscle, the alcohol at these temperatures will not extract sufficient lipoids to hold the cholesterin in solution after addition of salt solution. We would suggest, therefore, that after six or seven days' extraction in the ice box, the amount of coloring matter in the supernatant fluid be noted and if practically free from it, the extraction be continued at room temperature (in the dark) with frequent shaking. If on the ninth or tenth day of extraction the amount of coloring matter in the supernatant alcohol is still quite low, the extraction flask may be placed for some hours in the incubator before filtration of the alcohol.

We have for some time been attempting to devise a standard by which to judge the proper amount of coloring matter of the alcoholic extracts. Unfortunately, alcoholic extracts of different quantities of heart muscle frequently show different color ranges, thus rendering true comparisons difficult. Beginners with this test, however, would do well to have some approximate standard with which

Standard 1:

1. 0.5. gm. potassium bichromate ($K_2Cr_2O_7$) is dissolved in 100 c.c. distilled water (permanent standard solution).
2. 1 c.c. of above solution is mixed with 75 c.c. of distilled water.
3. 10 c.c. of Solution No. 2 is placed in a large test tube of about ¾ inch diameter. Into a tube of similar size is measured 10 c.c. alcoholic extract to be compared.

Standard 2:

1. An ammonium sulphate solution is prepared 1 c.c. of which contains 0.01 mgm. N.
2. 1 c.c. of this solution is measured into a large test tube about ¾ inch diameter, 8 c.c. of distilled water and 1 c.c. of Nessler's* solution added and mixed thoroughly.
3. Place 10 c.c. of alcoholic extract to be tested in a tube of similar size and compare colors.

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*Practical Physiological Chemistry, P. B. Hawk, 7th. Ed., Blackiston, p. 638.

to compare the amount of coloring matter of the alcoholic extract. For this purpose one may use some antigen which has been known to give good results in the hands of some workers, or either one of the preceding approximate standards. These are to be employed on the ninth or tenth day of the alcoholic extraction.

The 10 c.c. of alcoholic extract needed to compare with either one of the standards can easily be filtered from the extraction flask and if the extract is lighter than the standard employed, this amount is returned to the flask and extraction continued for several hours in the incubator. If, after that time, the extract is still weaker than the standard, extraction may be permitted to take place overnight in the incubator. By that time the antigen will be found in most cases to contain sufficient lipoids. The match between the extract and either of the standards need not be absolute, but they should approach one another. The value of employing a standard lies also in bringing about greater uniformity in the production of antigen.

It should be stated that an antigen which has been extracted for a given length of time in the incubator should be kept overnight at room temperature before cholesterinization. The incubator appears to extract certain elements which precipitate at room temperature. This precipitate should be filtered off before adding cholesterin.

The lack of constancy of icebox temperature in different laboratories early led us to investigate whether alcoholic extractions carried out for 10 days at room or incubator temperature might not produce antigens of as good potency as when ice box temperature is employed. The following experiments were carried out with a view of throwing some light on this problem.

A quantity of ground muscle prepared from beef heart was extracted with ether in the usual manner until free from coloring matter and dried. Ten gram quantities of dried material were then placed in three 100 c.c. Erlenmeyer flasks and 50 c.c. of 95 per cent alcohol added to each. Flask number 1 was extracted for 10 days in the ice box; flask number 2, for 10 days at room temperature and flask number 3, for 10 days in the incubator at 37.5° C. The flasks were kept in large containers to shut out the light. None of the flasks was shaken except after the addition of alcohol and just before filtration at the end of the 10 day extraction period. The amount of alcoholic extract filtered off in each case was approximately 35 c.c. Twenty-five c.c. quantities from each of these extracts were added to each of 3 other 100 c.c. Erlenmeyer flasks, 100 mgm. of cholesterin added to each, and mixed until dissolved. An identical experiment was carried out employing ground muscle prepared from pig heart. The comparative sensitiveness of both the beef and pig heart antigens at ice box, room and incubator extraction temperatures is recorded in Table I. Five dilutions of each serum were employed and the tests were carried out with 0.3 c.c. of each of the serum dilutions, and 0.05 c.c. of diluted cho-

Table I

Effect of Temperature of Extraction of Heart Muscle on Sensitiveness of Antigen

SERUM NO.	DILUTION OF SERUM WITH SALT SOLUTION	BEEF HEART EXTRACTION			SERUM NO.	PIG HEART EXTRACTION		
		ICEBOX	ROOM	INCUBATOR		ICEBOX	ROOM	INCUBATOR
1	1 + 1	++++	++++	++++	7	++++	++++	++++
	1 + 3	+++	++	+		++++	++++	++++
	1 + 7	+	+	±		++++	+++	++
	1 + 15	–	–	–		++	++	±
	1 + 20	–	–	–		–	–	–
2	1 + 1	++++	++++	++++	8	++++	++++	++++
	1 + 3	++++	++++	+++		++++	++++	++++
	1 + 7	++	++	–		++++	++++	+++
	1 + 15	+	±	–		++	++	+
	1 + 20	–	–	–		+	±	–
3	1 + 1	++++	++++	++++	9	++++	++++	+++
	1 + 3	+++	+++	+++		+++	++	++
	1 + 7	++	+	±		+	+	–
	1 + 15	–	–	–		–	–	–
	1 + 20	–	–	–		–	–	–
4	1 + 1	++++	++++	++++	10	++++	++++	++++
	1 + 3	++++	++++	+++		+++	+++	++
	1 + 7	+++	+++	++		++	+	+
	1 + 15	++	++	+		±	–	–
	1 + 20	+	+	+		–	–	–
5	1 + 1	+++	+++	+++	11	+++	+++	++
	1 + 3	++	++	++		++	+	–
	1 + 7	++	++	+		–	–	–
	1 + 15	+	±	–		–	–	–
	1 + 20	–	–	–		–	–	–
6	1 + 1	+++	+++	+++	12	++++	++++	++++
	1 + 3	+	±	–		++++	+++	+++
	1 + 7	–	–	–		++	++	+
	1 + 15	–	–	–		+	±	–
	1 + 20	–	–	–		–	–	–

lesterinized antigen in the usual manner. The results were read after overnight incubation.

It is evident from this table that ice box extraction results in a more sensitive antigen than either room temperature or incubator extraction. We have prepared antigens by extracting 5 hours and 24 hours in the incubator which gave fairly good results. Practically any mode of extraction will give antigens which will react positively with strongly positive serums. The problem, in our opinion, should centralize on the preparation of antigens which will be capable of reacting with weakly positive serums and judging from our observations so far, prolonged extraction (10 days) in the ice box combined with room temperature will produce a more sensitive antigen than a short extraction period in the incubator.

In regard to the keeping qualities of the antigen, we observed no variations in the potency of alcoholic extract antigens six months after extraction. We have no experience with such antigens beyond this period. In the case of cholesterinized antigen, however, we observed a slight diminution in potency on prolonged standing. We aim, therefore, to cholesterinize sufficient alcohol extract to last us only from three to four weeks. Thus in this laboratory where close to 3000 tests are made monthly, we cholesterinize about 40 c.c. of alcoholic extract at a time, which lasts about a month. The alcoholic as well as the cholesterinized extracts are kept in well stoppered bottles in the dark at room temperature. It occasionally happens during cold winter nights, that a small quantity of cholesterin crystallyzes out of solution. These crystals, however, can easily be redissolved by warming and gentle shaking.

THE DILUTION OF ANTIGEN FOR THE TESTS

In our early studies we diluted the antigen with the smallest amount of salt solution which produced a clear mixture. This mixture would gradually become slightly turbid, with the result that it was extremely sensitive to precipitation when added to positive serum. This led us at first to make our final readings after three to four hours' incubation.

It was felt, however, that the employment of antigen-salt solution mixtures showing slight turbidity involved the possibility of picking up false weakly positive reactions in the hands of some workers. Gradually we began to use antigen mixtures which were opalescent without showing the faintest trace of turbidity. These were somewhat less sensitive than the original antigen mixtures, and we were finally led to prolong the incubation period to from 16 to 18 hours.

When employing this incubation period it is of the utmost importance to use an antigen-salt solution mixture which shows no trace of turbidity. A turbid mixture will be likely to give false weak (±) reactions particularly with older serums. It does not matter if the mixture becomes turbid after its use in the tests, provided that it is entirely clear when added to the serum.

Different lots of cholesterinized antigen will behave somewhat differently after mixing with three parts of salt solution. Some will show little tendency toward turbidity or precipitation; others again will show a marked tendency to cloud soon after adding salt solution. We are inclined to think that the latter antigen will be likely to be more sensitive than the former, except that one must pay particular attention to an antigen which tends toward turbidity to avoid false weak reactions.

When employing an antigen highly sensitive to precipitation it is best to mix it with warm salt solution and keep it in a vessel of warm water until used. It will be found under these conditions that such an antigen-salt solution mixture will remain opalescent and clear for some hours. We would not, however, recommend the employment of warm salt solution for diluting antigens which do not show a tendency toward precipitation. Indeed, for such antigens we would urge the employment of salt solution kept in the ice box, since cold salt solution will be more likely to produce antigen mixtures sensitive to precipitation than warm salt solution.

We now turn to the problem of the keeping qualities of the antigen-salt solution mixtures. In our early work we were in the habit of mixing 5 c.c. of the cholesterinized extract with 15 c.c. of salt solution in a 25 c.c. cylinder and using the amount of this mixture required daily for the tests. This mixture was kept in the incubator and lasted from three to four days. We believed at that time that the sensitiveness of the antigen salt solution mixture was not affected by age. We have subsequently observed, however, that an antigen mixture will gradually become less sensitive on standing. Table II illustrates this finding.*

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*Some of these experiments were carried out by Mr. Ernest Burhans of this laboratory.

TABLE II

EFFECT OF AGE ON SENSITIVENESS OF DILUTED ANTIGEN

SERUM NO.	SERUM DILUTION WITH SALT SOLUTION	TIME OF USING ANTIGEN AFTER DILUTION WITH SALT SOLUTION					
		IMMEDIATELY	24 HR.	48 HR.	72 HR.	21 DAYS	28 DAYS
1	1 + 1	++++	++++	++++	++++	++	++
	1 + 3	++++	++++	++++	++++	++	++
	1 + 7	+++	++++	++++	+++	+	±
	1 + 15	+++	+++	+++	++	+	−
	1 + 20	+	−	−	−	−	−
2	1 + 1	+++	+++	+++	+++	+	−
	1 + 3	+	+	+	+	±	−
	1 + 7	±	±	±	−	−	−
	1 + 15	−	−	−	−	−	−
	1 + 20	−	−	−	−	−	−
3	1 + 1	++++	++++	++++	++++	++	+
	1 + 3	+++	+++	++	+	+	−
	1 + 7	+	+	±	±	−	−
	1 + 15	−	−	−	−	−	−
	1 + 20	−	−	−	−	−	−
4	1 + 1	++++	++++	+++	+++	±	−
	1 + 3	+++	+++	++	++	−	−
	1 + 7	+	±	±	±	−	−
	1 + 15	−	−	−	−	−	−
	1 + 20	−	−	−	−	−	−
5	1 + 1	++++	++++	++++	++++	+	−
	1 + 3	++++	++++	++++	++++	±	−
	1 + 7	+++	+++	+++	+++	−	−
	1 + 15	+	+	±	−	−	−
	1 + 20	−	−	−	−	−	−
6	1 + 1	++++	++++	+++	+++	+	−
	1 + 3	+++	+++	+++	++	−	−
	1 + 7	±	±	±	±	−	−
	1 + 15	−	−	−	−	−	−
	1 + 20	−	−	−	−	−	−

It is clear from this table that after mixing a cholesterinized antigen with salt solution there is a tendency toward a gradual diminution in sensitiveness. In our routine work, the extract antigen is mixed with salt solution and is used at any time within several hours. In a previous paper we advised waiting a half hour after mixing the antigen with salt solution before using in the tests. We feared that the immediate employment of a diluted antigen might lead to nonspecific reactions. On numerous occasions we employed such antigens immediately after dilution with good results. Our criterion for a correct mixture is that it is opalescent and that it shows no signs of turbidity, and we use it either immediately after mixing with salt solution or within several hours.

THE SERUM

The serum must be clear and inactivated for half an hour at 56° C. Serums which are turbid due to contamination are likely to give weakly positive reactions of a nonspecific nature. In this laboratory, all serums showing turbidity due to the presence of weak precipitates or contamination are checked before adding the antigen mixture, and in the final reading of results, if these serums show weak precipitations they are read as negative. It is interesting to note that when a serum originally turbid gives a strong precipitation reaction (++++ or +++), it will clear in the process of clumping of the precipitated particles. One will then see one or more clumps suspended in a clear fluid. It appears that the affinity of the specific precipitated particles for one another is so marked that in the process of clumping the nonspecific bacterial particles are also taken up.

The regular test consists of 0.3 c.c. of serum and 0.05 c.c. of diluted antigen. If 0.3 c.c. of serum is unavailable, lesser quantities may be employed provided a proportional amount of antigen is used. In this laboratory we use 0.2 c.c. of serum with 0.03 c.c. of antigen and in special cases, 0.1 of serum with 0.015 c.c. of antigen. The so-called micro-procedure discussed above must be carried out with especial care and is not recommended for routine work.

THE READING OF RESULTS

Most workers are accustomed to read precipitates by holding the tube on a level with the eye and looking through the medium. This method can be readily applied in reading ++++ or +++ reactions. These reactions are so marked that even those who have had no experience in reading precipitates can nevertheless see them readily. The weaker reactions, however, can easily be missed by this method of reading. The reason for this is that the serum is a heavy colloidal solution besides being frequently colored, and one cannot differentiate slight particles in it. The method which has given best results in our hands in the reading of weak precipitates is as follows: 1. Slant the tube to such an extent that it is almost horizontal. This causes the fluid to spread into a thin layer. 2. Hold the slanted tube some inches above the level of the eyes. 3. Focus against some dark object such as the lower part of a window shade. 4. Observe whether the thin layer of fluid is entirely clear or has fine particles evenly distributed.

The typical precipitate is suspended in the medium. Occasionally instead of being suspended, the precipitate will be settled on the bottom of the tube. If the reaction is specific it will be found on slanting the tube that the precipitate consists of clumps or particles of a typical character suspended in a clear medium. If the precipitate is stringy and clumps of various size appear to be attached to one another, the precipitate is bacterial in origin. In this case, the medium is invariably cloudy indicating bacterial contamination.

In this laboratory where the specimens are received through the mails and most serums are from three to four days old, we occasionally find precipitates settled on the bottom of the tubes and it is difficult to determine whether these precipitates are specific in character. The four plus and three plus reactions give little difficulty in this regard. The precipitates in these reactions even when settled on the bottom can be readily interpreted. In the case of weaker reactions we abide by the following criteria. (1) The serum must show no signs of contamination. (2) The precipitate should become distributed throughout the medium on slanting the tube. (3) The precipitate should consist of typical granules or flocculi. (4) If the precipitate consists of peculiar particles of various sizes and shapes the reaction is nonspecific. The differentiation between so-called typical flocculi or granules from nontypical precipitates can only be learned from experience.

The results of the precipitation tests should be read by two workers. During the second reading it is frequently found that some of the negative serums show clouding. This is due to the fact that many negative serums, particularly when several days old, have a fine sediment settled on the bottom of the tubes. The slight shaking which a given serum undergoes during the first reading tends to disperse the sediment throughout the medium and gives it a cloudy appearance.

In an earlier communication[1] it was suggested that the tubes which give questionable reactions be shaken and reread after 1 or 2 hours' standing. Shaking renders invisible some nonspecific doubtful precipitates and is thus of value in some cases. It must be remembered, however, that shaking also brings into suspension fine nonspecific sediments which in some instances, give the appearance of doubtful reactions.

Some antigens have a greater tendency to produce sediments in negative serums than others. Indeed, different quantities of antigen appear to have somewhat different characteristics, as is true in the case of Wassermann antigens. With some antigens the negative serums are in practically all cases entirely clear; with others, one will observe a comparatively large number of sediments, and with still others, one may find a considerable number of questionably weak reactions. The latter fortunately can readily be differentiated from true doubtful reactions after a little experience in reading the tests.*

THE INTERPRETATION OF SPONTANEOUS REACTIONS

It is occasionally desired to determine the presence of syphilitic infection in patients having to submit to emergency operations and in donors of blood for transfusion. It is therefore well to acquire the knowledge of reading spontaneous reactions. The typical reaction is unmistakable. After the proper mixing of antigen with serum one will observe clearly defined particles suspended in a clear medium within five minutes. One occasionally encounters, however, weak spontaneous reactions which are not quite typical. The following criteria will be found helpful in judging such reactions. 1. The specific spontaneous reaction shows on standing, a marked tendency toward the coalescing of the particles. If a weak reaction is observed about half an hour after mixing the antigen with the serum, the precipitate will be found to be considerably more pronounced with signs of clumping of the particles. 2. Centrifugation for several minutes will produce either several clumps or one large clump. These clumps will be suspended in the medium in most cases. Occasionally the clump will go to the bottom of the tube. Slight shaking of the tube will indicate at once the presence of one or more large clumps.

Different lots of antigen will show variation in the number of spontaneous reactions they are able to pick up. We have had antigens which gave these reactions with 90 per cent of the serums giving four plus Wassermann tests. Again some antigens gave such reactions with less than 50 per cent of serums giving four plus Wassermanns.

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*Since the preparation of this paper it has been observed that non-specific sediments in negative sera following incubation of serum and antigen are due to impurities in the extract. These impurities are caused, in most cases, by excessive contact of the extract with cork or rubber stoppers. It was furthermore observed that the addition of sheep cells to sera for removal of natural amboceptor will occasionally cause the formation of a non-specific precipitate, and should therefore be avoided.

Turbidity of the serum-antigen mixture is the first step in the formation of spontaneous precipitates. Shaking from one-half to two minutes will usually bring about precipitation in a turbid mixture. The same results will be obtained by short period (½ hour) of incubation.

It is interesting to note that we are apparently dealing with complete precipitation in these so-called spontaneous reactions. Incubation or centrifugation merely tends to clump the particles together, but does not, it appears, produce further precipitation.

A QUANTITATIVE TEST

When studying the effect of treatment it is occasionally desired to obtain more quantitative results of the precipitating power of a serum than that given by the routine test. In such cases we employ the regular test with two dilutions of serum with salt solution. Tube 1 contains 0.3 c.c. of undiluted serum; tube 2, 0.3 c.c. of serum diluted 1:5 and tube 3, 0.3 c.c. of serum diluted 1:10. The usual amount of antigen (0.05 c.c.) is added to each tube and the test completed in the usual manner. It is not uncommon in untreated cases of secondary syphilis for all three tubes to give four plus reactions. During treatment, however, the reactions gradually become weaker beginning with the highest dilution of the serum.

COMPARISON WITH WASSERMANN TEST

The Wassermann tests in this laboratory are carried out in duplicate employing an alcoholic antigen in one case and a cholesterinized antigen, in the other.[14] Although with certain quantities of antigen we obtained somewhat more sensitive reactions with the precipitation than with the Wassermann test, as a whole we believe that Wassermann tests carried out with a cholesterinized antigen are slightly more sensitive than the precipitation test. Even with this antigen specimens will frequently give stronger reactions with the precipitation than with the Wassermann test.

In comparison with Wassermann tests carried out with a noncholesterinized antigen, the precipitation test may be looked upon as more sensitive, although in this case also, one will occasionally encounter a specimen which gives a more sensitive reaction with the older test.

We are not as yet prepared to say why some antigens are more sensitive than others. The condition of the heart muscle may be an important factor. We are at present studying the differences in sensitiveness of antigens when prepared from heart muscle obtained from freshly slaughtered animals as compared with refrigerated hearts. Again it is possible that absolute alcohol may give better results than 95 per cent alcohol. We have observed little variation between these two types of alcohol. But our observations are based on qualitative rather than quantitative data.

Table III gives the results obtained with the Wassermann and precipitation tests on the bloods of 84 syphilitics at Jackson (Mich.) Prison under various stages of treatment. The tests were carried out on July 19, 1922, and form part of our routine records. The results according to the table give a general idea as to the fluctuations between the two tests.

THE RING TEST MODIFICATION OF THE PRECIPITATION TEST

Instead of mixing the serum and antigen and observing a precipitate, several workers suggested the possibility of adding the antigen to the serum carefully with a view to permitting the formation of a ''ring'' at the point of contact between the serum and antigen. Keim and Wile[15] observed such rings in the case of strongly positive serums. Herrold[16] suggested the employment of an antigen dilution of 1 and 12 (instead of 1 + 3) with salt solution and claimed good results in the case of definitely positive serums.

Although we were interested in developing a ring or layer test at a very early stage of our work with this precipitation reaction, we have felt that the ring which forms at the point of contact between the positive serum and antigen is, in most cases, too fine for definite interpretation. While studying the ring test in this laboratory, it was not uncommon, for example, for one worker to read a given test positive and for another to read it doubtful or negative. This is perhaps to be expected when one considers to

TABLE III

RELATIVE SENSITIVENESS OF WASSERMANN AND PRECIPITATION TESTS IN 84 CASES OF SYPHILIS IN VARIOUS STAGES OF TREATMENT

CASE NO.	RESULTS WITH		CASE NO.	RESULTS WITH	
	WASSERMANN TEST	PRECIPITATION TEST		WASSERMANN TEST	PRECIPITATION TEST
1	++	+++	43	+	+
2	+	+	44	++	+++
3	++++	++++	45	++	+
4	+	++	46	+	+
5	++	++	47	++++	++++
6	+	+	48	++++	++++
7	+++	++	49	++++	++++
8	+	+	50	–	–
9	+	++	51	++	+++
10	+	++	52	+	±
11	++	+++	53	++	++
12	+	+	54	+++	++
13	±	+	55	+++	+++
14	+++	+	56	++	++
15	++++	++++	57	++++	++++
16	±	±	58	+	+
17	++	++	59	+	+
18	++	++	60	++++	++++
19	++	++	61	+++	++++
20	+++	++++	62	++++	++++
21	+	++	63	+++	++++
22	–	–	64	++	+++
23	++	+	65	–	+
24	++++	++++	66	++++	++++
25	++++	++++	67	++	++
26	+	++	68	+++	++
27	++	+++	69	++++	++++
28	+++	++	70	+	++
29	++++	++++	71	++++	++++
30	+	+	72	++++	++++
31	+++	++++	73	++++	++++
32	+	++	74	++++	++++
33	–	+	75	++	+++
34	++	+++	76	+	++
35	+++	+++	77	++	++
36	++++	++++	78	+++	+++
37	++	+++	79	++++	++++
38	++++	++++	80	+++	+++
39	++	++	81	+	++
40	++++	++++	82	+	++
41	++++	++++	83	+++	++
42	++++	++++	84	++++	++++

what extent the angle of light plays a part in reading these ring precipitates.

We are inclined to believe that in the hands of some workers the ring test modification should give good results. Such a test, in

TABLE IV

COMPARISON OF RESULTS OF WASSERMANN, PRECIPITATION TEST AND RING MODIFICATION ON 162 SERUMS

SERUM	WASSERMANN	REGULAR PPT. TEST	RING MODIFICATION
1	++++	++++	±
2	++	++++	±
3	++++	++++	p*
4	++++	++++	p
5	++++	++++	p
6	+	++	–
7	+	++	–
8	++++	++++	p
9	++++	++++	p
10	++++	++++	p
11	+	+++	p
12	++++	++++	p
13	++++	++++	p
14	±	++	–
15	+++	++++	p
16	±	+	–
17	++	++++	±
18	+	+++	p
19	±	–	±
20	–	+	–
21	++++	++++	p
22	+++	++++	±
23	++++	++++	p
24	++++	++++	p
25	+++	++	–
26	++++	++++	p
27	++++	++++	p
28	++++	++++	p
29	++++	++++	p
30	++++	++++	p
31	++++	++++	p
32	++++	++++	p
33	+	++	–
34	++	+++	p
35	++++	++++	p
36	++	++++	–
37	±	–	–
38	++++	++++	p
39	±	+++	–
40	++++	++++	p
41	++++	++++	p
42	++++	++++	p
43	++	+++	–
44	+++	++++	p
45	++++	++++	–
46	++++	++++	–
47	++++	++++	p
48	±	++	–
49	+	–	–
50	+++	++++	p
51	–	++	–
52	++	++++	–
53	±	++++	±
54	++++	++++	p
55	–	–	±
56	++++	++++	–
57	+	++++	±
58	++++	++++	p
59	+	++++	p
60	++++	++++	p
61	++	++	–
62	–	–	p
63	++	++	–
64	+++	+++	p
65	+	–	p
66	–	–	p
67 to 162	–	–	–

*p=positive.

our opinion, should always be checked by the regular precipitation test or by the Wassermann test or both before reporting to physicians.

The findings recorded in Table IV were based on experiments with the ring test carried out by Miss Helen Gunn in this laboratory. It would appear that as a whole the test approaches some degree of accuracy compared with the Wassermann and regular precipitation test.

THE STATUS OF THE PRECIPITATION TEST

We are frequently asked, since the precipitation test is so simple, whether it might not be well for general practitioners to carry it out in their own laboratories. Our answer is No. The test is comparatively new. We have yet a great deal to learn regarding the various laws which govern it. In the hands of trained laboratory workers, it should give good results. Such workers could, for example, easily learn to recognize the typical precipitates and differentiate these from foreign particles which one occasionally encounters in serums. Laboratory workers are also more likely to examine comparatively large numbers of serums at one time and thus constantly gain more and more experience with this test.

Another question which occasionally comes to us is whether the precipitation test can safely be run independently of the Wassermann test. Although we have the utmost confidence in this test, we are nevertheless inclined to believe that at the present time it should be run parallel with the Wassermann. We have a record in this laboratory of 27,000 tests which gave comparable results with the Wassermann but we feel that a great many more comparable tests should be carried out by different workers before we can depend solely on the findings of this test. The main value of the precipitation test, as pointed out by Young,[17] lies in furnishing a check on the Wassermann. The complicated technic of the last test as well as its numerous sources of error renders a check of this kind of high value. On the other hand, where the Wassermann test cannot for any reason be employed, the precipitation test should prove of value in providing a laboratory diagnosis of syphilis and a check on treatment. In such cases one must keep in mind that whereas ++++ and +++ reactions are suggestive of syphilis, the weaker reactions should carry weight in diagnosis only in the presence of corroborative clinical findings.

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ADDENDUM

Since the preparation of this manuscript, we have evolved a check procedure for our precipitation test which is giving excellent results in our hands. Accordingly, each serum is examined by the method outlined in this paper as well as by the following modified procedure:

Dilution of Antigen for Tests.—1. A given amount of antigen (depending on number of tests) is measured into a small tube and an equal amount of salt solution is added to it either from a pipette or from another tube. 2. This is mixed and centrifuged for about 5 minutes—until the supernatant fluid is practically clear and a white precipitate is settled on the bottom of the tube. 3. The supernatant fluid is poured off and discarded and the amount replaced with salt solution. (Ex. 0.5 c.c. antigen is mixed with 0.5 c.c. saline and centrifuged. Supernatant fluid is poured off and 1 c.c. saline added.) 4. On mixing, the precipitate is redissolved in the salt solution forming a milky opalescent mixture with no trace of a precipitate. This mixture is then ready for use.

The Test.—Three-tenths c.c. of serum, previously inactivated for ½ hour at 56° C. is measured into a small tube and 0.05 c.c. of new antigen mixture added to it. The tube is shaken for about a minute. Practically all tubes will become slightly cloudy but those showing spontaneous reactions will show definite precipitations in clear serums. The final reading in this case also is taken after overnight incubation at 37° C. The incubation period, however, should not extend beyond 15-17 hours.

Reading of Results.—All tubes showing the presence of definite clumps or heavy precipitates are first picked out and set aside in a special rack. These are the ++++ and +++ reactions. The remaining tubes receive one c.c. of salt solution each and rack is gently shaken and permitted to stand about 10 minutes. The negative tests show opalescence, while the positive tests show the presence of precipitates.

The results of the two precipitation procedures check very closely. In isolated cases where there is disagreement, the average findings of the two methods are taken as the final result.

The employment of large tubes which will permit considerable evaporation of the serum during the incubation period, should be avoided. Agglutination tubes having an inner diameter of about 0.8 cm. will be found to give best results.

A CASE OF SYPHILITIC CHANCRE ON THE SCROTUM OF A PATIENT WITHOUT PENIS

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(Received for publication, January 15, 1923.)

THE following case is of interest, because it proves that even the loss of the penis does not preclude the possibility of being infected with syphilis through sexual intercourse.

At the beginning of April, 1922, a man aged fifty-four years was admitted to the Leipzig University Skin Hospital (Prof. Rille). At the age of ten he had in a jovial mood put a rubber ring round the root of his penis. The penis began to swell and after some time it was found necessary to amputate it, which was done at the Surgical Clinic, University of Leipzig. The patient is married and has three grown children. He would not say much about his private life, especially the sexual side of it. He had sexual intercourse in the normal position and the last time according to his words was in October, 1921. About the beginning of December he noticed an ulcer on the scrotum. He went to a doctor who treated him with fomentations only. As soon as an eruption appeared he was sent to our clinic.

An examination showed that the penis was altogether missing. The scrotum was enlarged and tight. The contents could be pushed into the body-cavity on the right side. The testes were normal. The skin of the mons pubis was drawn over the urethral orifice, on account of the dragging effect of a hernia, so that a short, loose organ existed. There were no signs of erectile tissue. Below the urethral orifice an ulcer, irregularly defined and of thumb size was found. The edges were not undermined and in consistency it was noticeably hardened; the surface was brownish-red with a serous shine (Fig. 1). The inguinal glands were the size of plums, indolent, very hard and easily movable. Around the anus were several fungous growths of lentil size and shaped like berries. On the skin

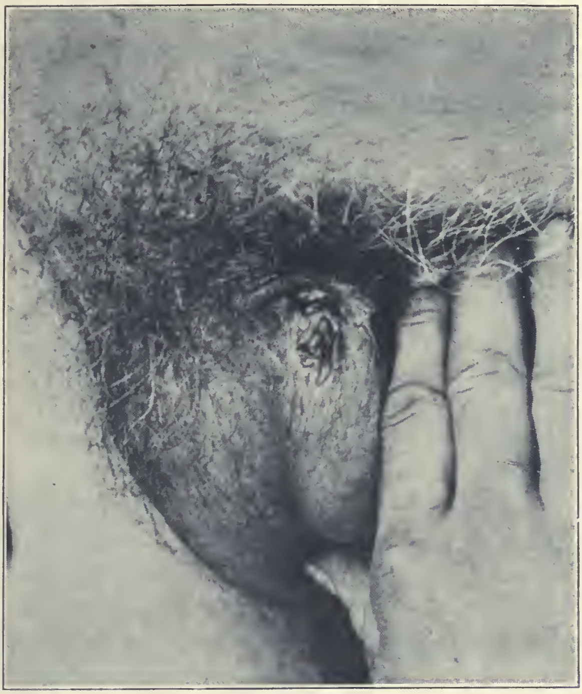

Fig. 1.

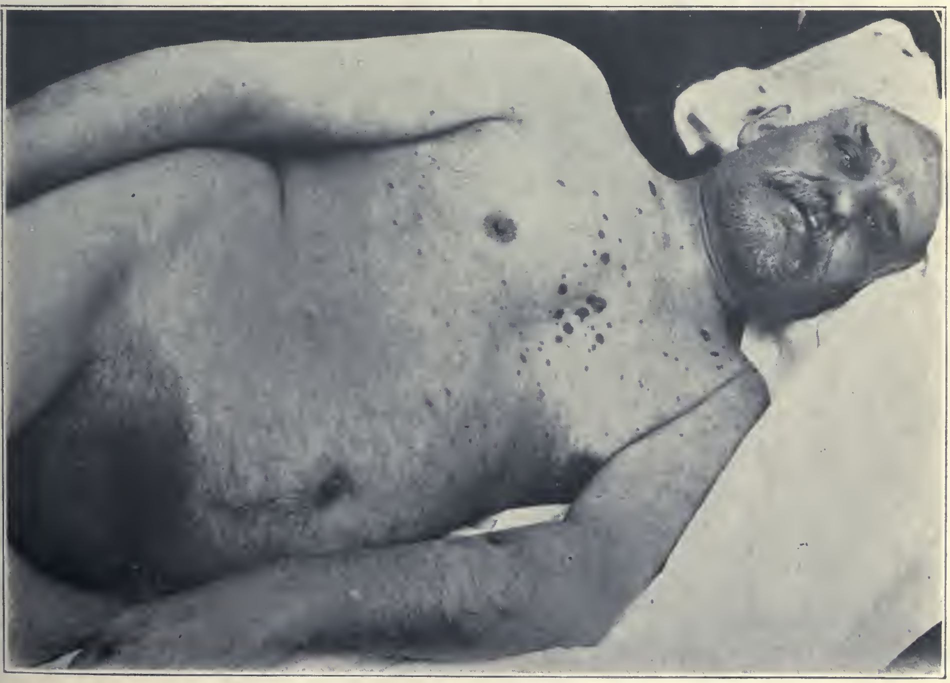

Fig. 2.

of the body and upper part of the chest were distinctly defined efflorescences, which varied in size from that of lentils to that of half-pennies and were located upon the surface of the skin, partly reaching above its surface. Those upon the chest especially showed deep brown discoloration. A few efflorescences showed formation of pustules. The lesions upon the neck and upper part of the chest showed ulcerous spots, distinctly defined (Fig. 2).

This is evidently a case of initial sclerosis of the scrotum, judging not only from the clinical information, but also from the condition of the inguinal glands. The long lasting persistence of the first stage of lues is most likely to be explained by the fact that the treatment was not the proper one and that the urine passing over the ulcer had an irritating effect. Most likely the skin of the scrotum was already injured, thereby rendering it all the easier for the patient to be infected.

The patient was treated with injections of neosalvarsan and cyrasal. The latter in solution I introduced into therapeutics, and is a mercury salt produced by J. D. Riedel, Ltd., Berlin. (*Munich Medical Journal.* Further experiences with Neosalvarsan-Cyrasal-Mischspritze.) Both solutions are mixed in the syringe, (on account of which I introduced the expression ''Mixing-Syringe'') and the mixture is injected intravenously. The syphilitic signs of the patient soon disappeared. After the fourth injection he was allowed to leave the hospital according to his own wish. But unfortunately he did not keep up the treatment regularly. At the end of April, 1922, when he left the hospital the Wassermann reaction was still four-plus. During September, 1922, I demonstrated the patient at the Congress of German Naturalists and Physicians. All he showed of his former disease was a scar on the scrotum. The other syphilitic signs had gradually healed, some of the lesions leaving pigmentation. The Wassermann reaction was negative.

Abstract of Current Syphilis Literature

It is the purpose of this JOURNAL to review so far as possible all literature on syphilis as it appears in other medical periodicals and to present it in abstract form. Authors are requested to send abstracts or reprints of their papers to the Associate Editor, Dr. Grayson E. Tarkington, Dugan-Stuart Bldg., Hot Springs National Park, Ark.

GRAYSON E. TARKINGTON, M.D., EDITOR.

Neurosyphilis among the Chinese.—William G. Lennox, Peking, China. Archives of Neurology and Psychiatry, 1923, vol. ix, p. 26.

Testimony of individual observers and reports of general hospitals agree that in China syphilis is relatively more common and neurosyphilis relatively less common than in America. One explanation for this apparent racial discrimination is the probability that, for reasons named, many cases of neurosyphilis among the Chinese have been overlooked. In a teaching hospital in Peking, search for these cases revealed a proportion comparable with that found in teaching hospitals in America. An unusual proportion of the Chinese patients have cord lesions of vascular origin. Sixty-five cases of neurosyphilis are reported in which spinal fluid examination confirmed the clinical diagnosis.

Studies in Syphilis.—N. Hamilton Fairley, Melbourne, Australia. The Medical Journal of Australia, 1921, vol. ii, p. 587.

The various protocols indicate that syphilis in the hospital population (especially in the married section) is largely manifesting itself in its tertiary, latent and familial aspects. While venereal clinics are making a progressively more serious effort to deal with acute syphilis, no organized movement is being attempted to combat the great problems of familial and latent syphilis, especially in women. The outstanding need, as we see it, is for clinicians to treat syphilis as a family disease, in whatever hospital the disease is diagnosed. The author's scheme, which is diagramatically represented by lantern slides, involves cooperative action on the part of the different metropolitan hospitals in the diagnosis and treatment of syphilized families. For example, if at the Alfred Hospital, a married male is found to have syphilis, then his wife and family should be clinically examined and have a blood test made. If any are found to be syphilitic, they should be distributed as circumstances demand to special hospitals for treatment; if pregnant, the mother should be treated in an antenatal obstetric clinic; the children under fourteen years should attend a children's department. Similarly, where children are found to be syphilitic at the Children's Hospital, the father and mother should be examined; also any older children. They could then be distributed to different hospitals for treatment.

Acquired Syphilis by Genital Chancre in Male Children, with Report of a Case in a Boy Five and One-half Years.—Mihran B. Parounagian and Herman Goodman, New York. Archives of Pediatrics, 1922, vol. xxxix, p. 651.

A rare instance of genital contagion of syphilis in a boy of five and one-half years is reported. The sequence of syphilis was typical. There was a chancre of the sulcus, generalized eruption, mucous patches, positive Wassermann, and ready response to arsphenamine. The source of contagion was either a prostitute residing in the same building as the patient, or one of her patrons.

Syphilis Transmitted to the Third Generation.—C. F. T. East, London. The Lancet, 1923, vol. cciv, p. 128.

The case described would appear strongly to support the evidence that congenital syphilis can be transmitted to the second generation.

Syphilis of the Mouth.—William Allen Pusey, Chicago. The Journal of the American Medical Association, 1922, vol. lxxix, p. 1285.

The skin and the mouth are the structures for which syphilis shows its greatest predilection, and the predilection is quite as great for the mouth as for the skin. About 60 per cent of all extragenital chancres are chancres of the mouth. Chancres of the mouth occur with vastly greater frequency on the lips; after that, they occur with about equal frequency on the tongue and tonsils. Vastly more frequent than any other eruption of secondary syphilis in the mouth are the several forms of mucous patches. Mucous patches are nearly always accompanied by other evidence of syphilis. Condylomas are rare lesions about the mouth. They occur occasionally at the angles and very exceptionally in the floor of the mouth. The tongue, in addition to being a frequent site of gummas, is attacked even more frequently by an interstitial syphilitic infiltration, which is analogous to the sheetlike interstitial infiltrations of syphilis that occur in the viscera, and in connective tissue and muscular structures such as the aorta. Smooth atrophy of the tongue is a result of interstitial glossitis. Superficial glossitis is probably the most frequent cause of syphilitic leukoplakia. Congenital syphilis of the mouth differs in no essential feature from the acquired disease. The treatment of syphilis of the mouth is the treatment of the disease in general.

Syphilis of the Uterus.—J. C. Sosnowski, Charleston, S. C. Surgery, Gynecology and Obstetrics, 1922, vol. xxxv, p. 610.

A series of 87 cases was studied. The special uterine pathology is studied step by step. Considering the pathology, the symptomatology is rather obvious.

The general symptoms are commonly known. The uterine symptoms are often ascribed to other causes. The so-called tertiary syphilitic affections of the uterus may in some cases be mistaken for carcinomata, and treated as such. Some of the remarkable recoveries after operation on extensive, apparently malignant, growths may be accounted for by this.

Syphilis of the Testicle Confined to the Epididymis.—A. Reith Fraser, Aberdeen, Cape Town, S. Africa. The British Journal of Dermatology and Syphilis, 1922, vol. xxxiv, p. 195.

Interstitial epididymitis occurred eighteen years after the initial infection. The condition was bilateral. The one side was acute and the other chronic. There was a unilateral implication of the vas. The prostate and seminal vesicles were not implicated. Both testes were normal. The condition responded rapidly to treatment. There was no other evidence of active syphilis.

Syphilis of the Lung.—W. T. Munro, London, Eng. The Lancet, 1922, vol. cciii, p. 1376.

Acquired syphilis of the lung may occur in three conditions: (1) gummata, (2) fibroid induration, (3) areas of consolidation and catarrh. Fibroid induration is the most common. In these cases the initial lesion would appear to be at the right base. No patient of this type was under 35 years of age. The shortest time between infection by the spirochete and symptoms referable to the chest was three and a half years. Antisyphilitic treatment in the early stages is to be recommended, but when bronchiectasis is well established treatment is not likely to lead to improvement. Two cases of focal disease were found. Both improved on treatment. This condition will occur in younger patients. Congenital syphilis of the lung may be common, and responds to treatment.

The Incidence of Syphilis in Hypothyroidism and Myxedema in Children.—Murray B. Gordon, Brooklyn, N. Y. New York Medical Journal, 1922, vol. cxv, p. 350.

There is little in the literature on the part syphilis can play in the causation of myxedema or hypothyroidism in children. Future studies of these conditions should be directed along lines which include serological and clinical investigations of patient and parents. No endocrine case report should be considered complete unless all modern scientific aids have been utilized in its study. Endocrinology will never be a scientific study until it is attacked by scientific methods. The results obtained in this series indicate that syphilis is not of great etiological importance in the causation of either myxedema or hypothyroidism in children. It is however, possible for syphilis to attack the thyroid gland with the production of these conditions. The presence of a mental deficiency in three of the five positive cases is significant of the predilection of the Spirochæta pallida for the brain and nervous system.

Recognition of Congenital Syphilitic Inflammation of the Long Bones.—Hubert M. Turnbull, London. The Lancet, 1922, vol. ccii, p. 1239.

Congenital syphilitic disease of bone is not a general systemic condition, but is due to the local presence of spirochaetae. The older the child, the fewer are the portions of bone affected. In the fetus the infection tends to be widespread, but it is not necessarily universal. When several bones are affected, the lesions are greater and more conspicuous in some bones than in others. It is advisable, therefore, in each case to examine as many bones as possible. The femur, tibia, humerus, and ribs are sites of election; the femur and ribs are easy of access, and should be examined in all cases.

Associated Syphilis and Tuberculosis.—A. L. Bramkamp, California. California State Journal of Medicine, 1923, vol. xxi, p. 52.

Syphilis of the lung is less rare than has been thought. Syphilis and tuberculosis are also more often associated in chronic fibroid lesions of the lung than is generally recognized. The effect of the association of syphilis with tuberculosis in the lung varies, depending largely on the stage and the degree of activity of each. Antisyphilitic treatment is indicated only when there is reason to believe, first, that syphilis is directly affecting the general health of the patient or is producing dangerous local lesions; or second, when the two processes are associated in the lung and the usual methods of treatment for tuberculosis fail to bring about satisfactory improvement. Treatment of associated syphilis and tuberculosis must be individualized and carried out with due caution as to remedy selected, dose, interval and duration of treatment. Mercury, arsphenamine and iodides are all capable of great good as well as of great harm, immediate or late. Mercury is probably less dangerous than the arsenical.

Report of a Case of Nodular Disseminated Nonulcerative Syphilides.—P. Gutierrez, Manila, P. I. The Journal of the Philippine Islands Medical Association, 1922, vol. ii, p. 293.

A case is presented with rare late manifestations of syphilis. These manifestations are in the form of nodules, unusually large in size and nonulcerative. That the individual has had syphilis and that the lesions are syphilitic in nature are evidenced by the history, the Wassermann reaction, the histological findings, and their reaction to treatment.

Syphilitic Backache.—Warren Thompson, Omaha, Neb. The American Journal of the Medical Sciences, 1922, vol. clxiv, p. 109.

Backache as a chief complaint may be due to syphilitic spondylitis, and although the condition is rare it should be considered as a possibility in every indefinite case of backache. Syphilis may involve any part of the spine; the most frequent location, according to the literature, is in the cervical vertebrae.

The pathology is similar to syphilis of bone elsewhere in the body. The nervous manifestations depend on the part of the vertebral column involved and the extent of the morbid process. Syphilitic spondylitis presents no definite clinical picture, the diagnosis being made chiefly by (1) roentgen-ray, (2) evidence of syphilis elsewhere in the body, (3) the Wassermann test, and (4) the therapeutic test.

Syphilitic Headache.—Irwin C. Sutton, Anaheim, Calif. California State Journal of Medicine, 1923, vol. xxi, p. 3.

Aside from the severe headache seen so often in early syphilis, there is little that is typical in the symptomatology of syphilitic headache. Syphilis should be suspected in all instances where head-pain is a prominent and chronic symptom. Headaches which do not disappear on the correction of refractive errors, to the removal of foci and the draining of sinuses, nor to that procedure known as a "cleaning out of the intestinal tract" should arouse the suspicion in the mind of the attending physician that syphilis may be present, and an examination for other signs of syphilis should be made.

Syphilis of the Internal Ear.—W. T. Salmon, Oklahoma City. The Journal of the Oklahoma State Medical Association, 1922, vol. xv, p. 328.

Syphilis cannot reach the labyrinth or brain except through the blood and other fluids of the body but it often does without any other symptom except the initial sore which may heal without treatment or recognition. Owing to the improved method of diagnosis this condition is thought to be much more prevalent than was formerly supposed, and a deafness without an apparent middle ear trouble, showing a marked shortening of bone conduction should at least be put down as a suspicious case. There are a variety of diseases that may cause the sudden loss of hearing and a diagnosis should not be made upon this one condition. The symptoms caused by syphilis of the inner ear may be unilateral or bilateral, but upon close examination, it may be found that the hearing is deficient in both ears but more marked in one than the other. In spite of a negative Wassermann and spinal fluid, the pathological changes responsible for the loss of hearing may point to syphilis. The prognosis in the hereditary form is always grave and the same may be true in the acquired form unless appropriate treatment is instituted at the early stage before injuries to the structures compressed become well advanced. Iodide of potash, given in heroic doses, often yields a better result, until certain stages are passed, than any other remedy given. Many cures have been recorded where there had been a long and repeated treatment with arsphenamine.

The American Journal of Syphilis

A QUARTERLY JOURNAL DEVOTED TO THE
STUDY AND PREVENTION OF SYPHILIS

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Original Articles

PRACTICAL OBSERVATIONS ON SYPHILIS. VI

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Section 19

(Received for publication, March 21, 1923)

DIAGNOSIS

ONE rule which the author attempts to impress upon his students is the following: Be quick to suspect syphilis; be slow to diagnose syphilis. At the present time entirely too much stress is laid upon the Wassermann reaction. As a matter of fact the diagnosis of this disease is often an extremely difficult one, and there are a number of procedures which are more or less helpful in establishing a correct diagnosis. The following outline will show what these procedures are:

(1). The personal history.
(2). The history of the family or associates.
(3). Examination of the family or associates.
(4). Physical examination of the genitals.
(5). Examination of the skin and mucous membrane.
(6). Examination of the bones, lymph nodes, spleen, liver, eyes, ears, teeth and testicles.

(7). Special examination of certain internal organs.
(8). A careful cardiovascular examination.
(9). Neurologic examination.
(10). Ophthalmologic examination.
(11). Examination of the ear.
(12). Cystoscopic examination.
(13). The Wassermann reaction.
(14). Other serological tests.
(15). The Luetin reaction.
(16). Examination of the spinal fluid.
(17). Dark-field examination.
(18). Demonstration of organisms by stains.
(19). Animal inoculation.
(20). Levaditi stain.
(21). Histologic examination.
(22). Roentgen ray examination.
(23). Therapeutic test.
(24). Operation.
(25). Autopsy.

PERSONAL HISTORY

The personal history of patients must always be accepted with much caution; for some will attempt to deceive the physician, and others are ignorant regarding the real nature of their trouble. Some will magnify and some will minimize affections. Even with a careful history it is frequently impossible to be certain of syphilis. In addition it is well recognized that the initial and secondary stages may be so slight that it is natural for the disease to be unsuspected by either the patient or the physician.

HISTORY OF THE FAMILY OR ASSOCIATES

The history of either the family or associates may or may not be helpful for the reasons that have already been mentioned. Naturally a family history is taken when one suspects congenital syphilis. It is good practice invariably to ask concerning any miscarriages on the part of the wife, and the early history of the children.

EXAMINATION OF THE FAMILY OR ASSOCIATES

The examination of the family or associates may or may not throw considerable light upon the case in question. If a mother has active syphilis, the child may reasonably be suspected of having the disease. The existence of lues in one member of a married couple should lead us to search for it in the partner. At the same time it is often surprising how one can escape repeated exposures. In the old days we heard much of "diagnosis by confrontation." A man who has a suspicious lesion after having consorted with a woman who has a definite active syphilitic lesion has good reason to suspect that he has acquired syphilis. At the present time this method is chiefly used before the appearance of the initial lesion.

EXAMINATION OF THE GENITALS

The physical examination of the genitals must never be neglected. Ordinarily the scar of a chancre is a rather small affair, but this is not necessarily the case. In the female, the cervix should never be neglected. The mere existence of a scar upon the genitals does not make the diagnosis of syphilis certain, for it may be due to a chancroid, various superficial diseases, or trauma.

EXAMINATION OF THE SKIN AND MUCOUS MEMBRANE

A careful examination of the skin and mucous membrane is extremely important, and should always be done in a good light and with the patient stripped. A faint roseola is frequently overlooked in a dark room. During the fulminating stage an experienced dermatologist can frequently diagnose syphilis at a glance. The annular syphilides are absolutely characteristic. Broken down gummata and certain of the nodular eruptions are also pathognomonic to the trained eye. Examination of the mucous membrane may be extremely suggestive. For instance perforation of the palate is indicative of syphilis. Mucous patches can usually be recognized but may be imitated by Vincent's angina, herpetic vesicles, or occasionally by erythema multiforme.

EXAMINATION OF THE BONES, LYMPH NODES, ETC.

A routine examination must always be made of the bones, especially of the tibiae or clavicles. It is of course, true that nodes upon the tibiae can arise from causes other than syphilis, but this is infrequent. The frontal bones and the sterno-clavicular articulations should never be overlooked. The joints should likewise be inspected for any swelling and palpated for any tenderness. The lymph nodes should always be felt; it is usual to begin with the posterior cervical nodes and examine in the following order: the anterior cervicals, the submental, the axillary, anterior axillary, epitrochlear and inguinals. Enlargement of the posterior cervical and epitrochlear nodes, especially if bilateral, is an important point in favor of syphilis, although not absolutely a certain sign. Search should always be made for an enlarged liver and spleen. As a rule these are more apt to be enlarged in congenital than in acquired syphilis, but they may be frequently palpated in any type of the disease. The eyes should be inspected for iritis, irido-cyclitis or any paralysis of the eye muscles. The hearing should be tested. In cases of suspected congenital syphilis a search must be made for Hutchinson's teeth, or mulberry molars, and lastly the testicles should be examined.

SPECIAL EXAMINATION OF CERTAIN VISCERA

Frequently it is necessary to examine with particular care certain of the viscera. For instance it may be necessary to distinguish between carcinoma and a syphilitic ulceration of the rectum, or between malignancy and gummous changes in the stomach.

CARDIOVASCULAR EXAMINATION

A careful cardiovascular examination is of great importance. It is now generally recognized that syphilis is very prone to attack both the heart and larger arteries, although other vascular organs may also be affected. The prevention of aortitis, aneurysm, myocarditis, angina pectoris, and aortic insufficiency is one of the gravest and least recognized problems of the syphilologist of today. Cardiovascular examination should be made with special emphasis laid upon a systolic murmur in the aortic area and any possible myocardial weakness. In case of any doubt fluoroscopic examination should always be made of the aorta.

NEUROLOGICAL EXAMINATION

Neurological examination is of the utmost importance, for by it we are usually able to suspect involvement of the central nervous system. There is almost no limit to a complete nervous examination but such is usually not required as a routine in syphilis. The following examination will usually suffice: The eyes should be examined for the size, inequality and reaction of the pupils. Hearing should be tested. The jaw, elbow, abdominal, cremasteric, patellar and tendo Achilles reflexes must always be examined. The simple tests of sensation and coordination may be important. Tremors and the Romberg sign must always be tested for.

OPHTHALMOLOGIC EXAMINATION

A special examination by a skilled ophthalmologist will frequently reveal syphilis in unusual cases. At times when a spinal fluid examination is negative a skilled ophthalmologist may be able to diagnose such a condition, from an examination of the eye grounds. During the work of the author on one of the Medical Advisory Boards he was very much struck by the fact that the ophthalmologist upon the Board recognized the existence of syphilis in practically every case, and that he unearthed many instances of the disease which were negative to a general physical examination.

EXAMINATION OF THE EAR

Examination of the ear is probably not of any striking value from a diagnostic standpoint, despite the claims that have been made for certain tests.

CYSTOSCOPIC EXAMINATION

Cystoscopic examination not infrequently reveals a trabeculated bladder which usually occurs with tabes, although it may be found in other diseases of the cord. Where a syphilitic patient shows any urinary disturbances a cystoscopic examination should always be made.

THE WASSERMANN REACTION

In 1906 Wassermann, Neisser and Bruck published a description of what is now generally known as the Wassermann Reaction. Naturally there have been various claims as to priority, but these need not interest most of us. Suffice it to say that the reaction is a complement-fixation test and is the direct result of Bordet's discovery of the principle of complement-fixation. In view of the manifold substances required in the test there have been thousands of modifications, but this is no place to discuss them. However, at the present time it may be safely said that any test should be performed with both an alcoholic and a cholesterinized antigen. The ice box fixation method is a very delicate one and may be of some value in following the treated cases. In many quarters the Kolmer test is spoken of very favorably and it is probable that for the time being at least this will prove to be one of the best methods. The Hecht-Weinberg modification is used in a few laboratories, but has never gained great popularity, despite the claims made for it.

As a matter of fact it is probable that more attention should be paid to the laboratory worker than to the method employed. More than once I have split one specimen of blood into four parts and sent it to four workers; all supposedly employing the same technic, and have received results varying from negative to complete positive. It is these unfortunate occurrences that discredit any test, when as a matter of fact the technician, and not the test is in error. Fortunate it is that the vast majority of workers are much more apt to err upon the side of reporting negative than of reporting false positives. Hence, it behooves the careful clinician to choose the serologist with the same care that he would choose a surgeon to perform a difficult operation upon his own child.

Even in competent hands the Wassermann test has certain definite limitations and certain very definite advantages. It is but one of the many signs of syphilis, and hence makes an excellent servant, but a hard master. It is unfortunately true that thousands of physicians put infinitely more faith in the Wassermann reaction than they do in all other laboratory and clinical methods combined, and faith in any one method to the exclusion of all others naturally leads to grievous error.

A frank, reliable positive Wassermann reaction in the United States means syphilis, yaws, or leprosy; the latter two diseases are extremely rare and for all practical purposes may be disregarded. Exceptionally a so-called false positive is reported but under ordinary circumstances the reaction is weak and if repeated in several weeks will be found to be negative.

A negative Wassermann reaction in syphilis is frequently found and hence the mere occurrence of such a reaction means very little except in the acute secondary stage where it is almost invariably positive. The following outline will reveal some of the conditions in which the Wassermann reaction is negative in the presence of active syphilis:

1. Blood withdrawn shortly after the individual has consumed 100

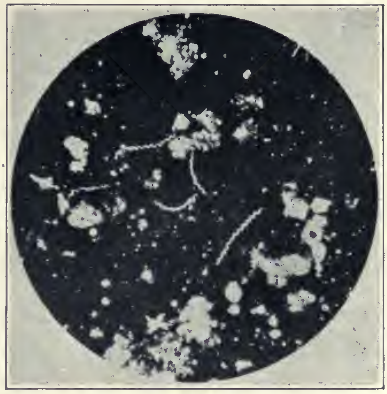

Fig. 52.—The Treponema pallidum can be best recognized by the dark field illuminator. (Courtesy of the E. Leitz Co.)

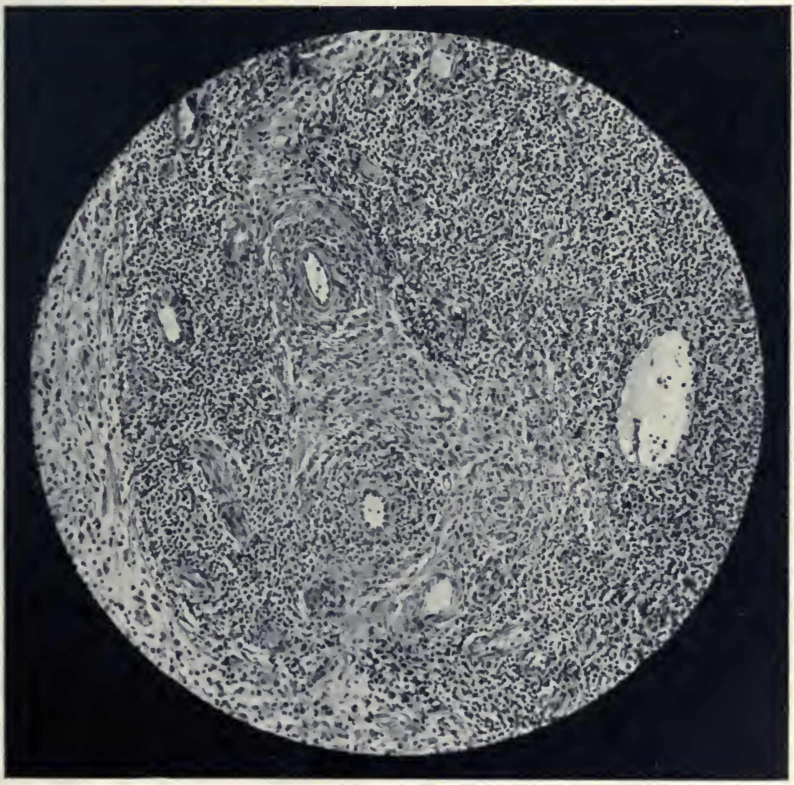

Fig. 53.—The section from which this photograph was made was taken from the edge of an early chancre. Notice the thickening of the blood vessel walls and the perivascular infiltration. (Collection of Drs. Fordyce and MacKee.)

c.c. of alcohol will often cause a positive Wassermann to become negative.

2. The growth of certain bacteria in serum may cause a negative reaction, and incidentally an occasional false-positive.

3. There may be variations in amount of a complement inhibiting substance.

4. Blood taken from the umbilical cord is frequently negative.

5. During the first four or five months after birth a child with congenital syphilis may give a negative reaction.

6. During the first two weeks of acquired syphilis the Wassermann reaction is usually negative.

7. In the late stages of the disease, especially in the inactive cases the reaction is negative in at least 25 per cent.

8. Many laboratory reports are not sufficiently delicate, hence it should be obvious that a negative reaction means very little, although repeated negative reactions may have a slight presumptive value. Especially should it be borne in mind that the blood reaction is frequently negative despite marked changes in the central nervous system. This point cannot be too strongly stressed.

By the end of the first week, after the appearance of an initial lesion the reaction is partially positive in about 25 per cent of all cases; by the end of the second week it is positive in about 40 per cent; by the end of the third week in 60 per cent, and by the end of the fourth week in about 80 per cent. During the first two or three days of the secondary rash a negative reaction is obtained in possibly 5 per cent of all cases, but after the rash has been out for one week the reaction should be positive in at least 99 per cent of the patients. During the late stages of syphilis the findings vary considerably. Cases which can be easily recognized clinically will yield positive findings in nearly 90 per cent in all instances, but with neurosyphilis the percentage of negative bloods is much higher than this. Where there are no clinical signs of syphilis the blood is probably negative in 25 or 30 per cent of all cases.

Just as too much stress is placed upon the Wassermann reaction as a diagnostic procedure, so is too much stress placed upon the reaction as a therapeutic guide. On the one hand many physicians will stop treatment just as soon as the reaction becomes negative, and on the other hand many will continue to treat a late case almost indefinitely in the hopes of producing a negative reaction.

As a matter of fact a certain minimum amount of treatment should always be given, no matter what the reaction may be. It is often an act of supreme folly to give 50 or 60 intravenous injections in the hopes of making Wassermann-negative a case that has had syphilis for 20 years. Patients have been educated to believe that a Wassermann reaction is the surest index of their disease and this certainly is not true, for physical signs and symptoms are infinitely more important. One general concession may be made and that is that it is always desirable to give sufficient treatment to produce a negative test, provided that this can be done within reasonable limits.

The so-called Wassermann-fast cases are especially interesting. In the majority of instances it is probable that an infection of the nervous system is responsible, and in every case where the reaction persists a spinal test must be done. At times, however, syphilis of the liver, the aorta, or other organs may be responsible for a persistent reaction.

The expression ''Provocative Wassermann'' is used to indicate a negative reaction that becomes positive shortly after the intravenous injection of arsphenamine. The test is done as follows: An ordinary intravenous injection of arsphenamine is administered and on each day for six consecutive days the blood is tested. The value of this test is much discussed, but generally speaking it may be said that there is a healthy skepticism concerning it. My own results with it have been extremely poor, and it should never be forgotten that a neurorecidive may follow its use as in one of my cases.

OTHER SEROLOGICAL TESTS

Attempts have been made from time to time to use other serological tests than the Wassermann reaction. Among those which must be mentioned are the Meinicke, the Sachs-Georgi, the Bruck test, the Vernes phenomenon and the Kahn. All of these are interesting and deserving of further study. At times they seem more delicate than the Wassermann reaction but at the present as final evaluation cannot be made, the general practitioner will do well to stick to the Wassermann reaction.

THE LUETIN REACTION

Noguchi first perfected an allergic reaction that was of value in syphilis and that compared with the cutaneous tuberculin tests.

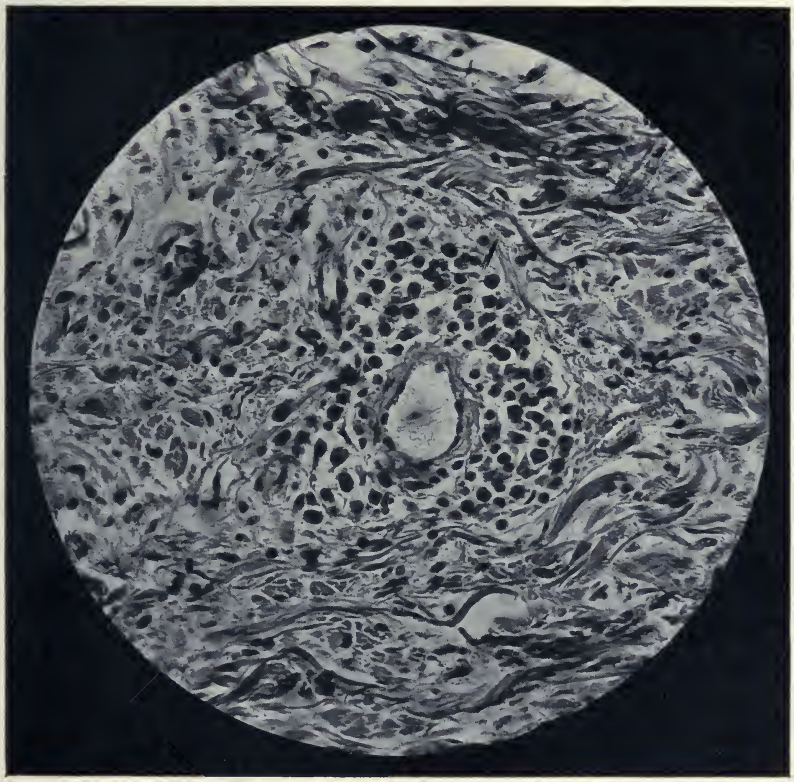

Fig. 54.—This illustration shows the perivascular infiltration occurring in a secondary skin lesion. The plasma cells show very distinctly. (Collection of Drs. Fordyce and MacKee.)

Luetin consists of pure cultures of Treponema pallidum. It is made in a way similar to ordinary bacterins. Its sterility is tested both culturally and biologically.

In testing an individual an all-glass very fine syringe, graduated in one-hundredths of a cubic centimeter is employed. For an adult 0.035 c.c. of luetin is drawn into the barrel and then an equal amount of sterile normal solution, and the two are mixed and then injected into the skin, not into the subcutaneous tissue. A slight raised wheal must be produced or the injection is too deep. This will disappear in less than an hour. In children about three-fifths of the adult dose is employed.

Reactions are of the following type, negative, papular, pustular, hemorrhagic and delayed.

In case of a negative reaction the following phenomena are usually displayed; at the end of a few hours there is a slight red macule, or in some instances a maculopapule that disappears in less than three days; this is due to irritation and trauma and is not specific. In other instances there may be absolutely no reaction whatever.

In primary syphilis it is rarely positive; in secondary syphilis it is positive in 47 per cent of the cases; in late syphilis it is positive in about 80 per cent.

Unfortunately the ingestion of iodides will usually result in a false-positive. In addition many of the samples of luetin are totally inactive, as shown by Alderson. The result has been that the reaction has fallen into disuse. Possibly one of the chief values of luetin is one of the criteria of cure.

EXAMINATION OF THE SPINAL FLUID

The examination of the spinal fluid has already been discussed in the Section on Syphilis of the Nervous System. However, attention should again be called to the fact that an examination of the spinal fluid will frequently reveal neurosyphilis where it is not suspected from either physical signs, or from examination of the blood. Latent neurosyphilis is gradually assuming great importance in the work of the syphilologist, the neurologist, and the internist. A diagnosis of neurasthenia should never be made without a spinal fluid examination.

Four tests are usually done upon the fluid; the Wassermann reaction upon various dilutions of the fluid, a cell count, a test for globulin, and a gold sol reaction. Again it should be emphasized that lumbar punctures should not be made in the office or dispensary, but that patients should be hospitalized for at least forty-eight, and preferably fifty-six hours.

DARK-FIELD EXAMINATION

For a satisfactory examination with the dark-field illuminator it is necessary to have clear serum, and but very few blood cells. Usually a chancre is so tender that it cannot be squeezed hard enough to exude clear serum. However, if the outer surface be gently cleansed, preferably with a little alcohol, this allowed to dry, and then the surface gently scratched with a knife a little serum will frequently exude; if it does not, suction may be made with a small pipette. If it is still impossible to obtain satisfactory material the lesion should be punctured at the edge; after blood has ceased flowing a little serum will usually exude. In very stubborn cases blood may be collected, allowed to clot, and then the clear serum used.

The apparatus consists of the following: a microscope with a good oil immersion lens, and with a rubber funnel diaphragm screwed in just above the lens, a special condenser or dark-field illuminator, which replaces the ordinary substage condenser, a special powerful light, preferably a small arc lamp with biconvex lens, and thin slides and cover-slips. The light is focused by means of the usual mirror on the microscope. The dark-field is so constructed that the direct rays of light are cut out by an opaque stop, while the peripheral rays are reflected from the sides of the instrument and are focused at a spot which will strike the top of a glass slide, laid on the instrument. This illuminates all objects brilliantly against a dark background. A drop of immersion oil must be placed upon the dark-field and the slide pressed against this, then oil is also placed on the upper surface of the cover-slip just as in other oil immersion work.

The dark-field has several great advantages: in the vast majority of instances it will enable an absolute and early diagnosis of syphilis to be made within a very few minutes. It must always be borne in mind that if a lesion has been treated with antiseptics so many of the treponemata may have been killed that they cannot be demonstrated; in such instances it may be necessary to prevent the patient

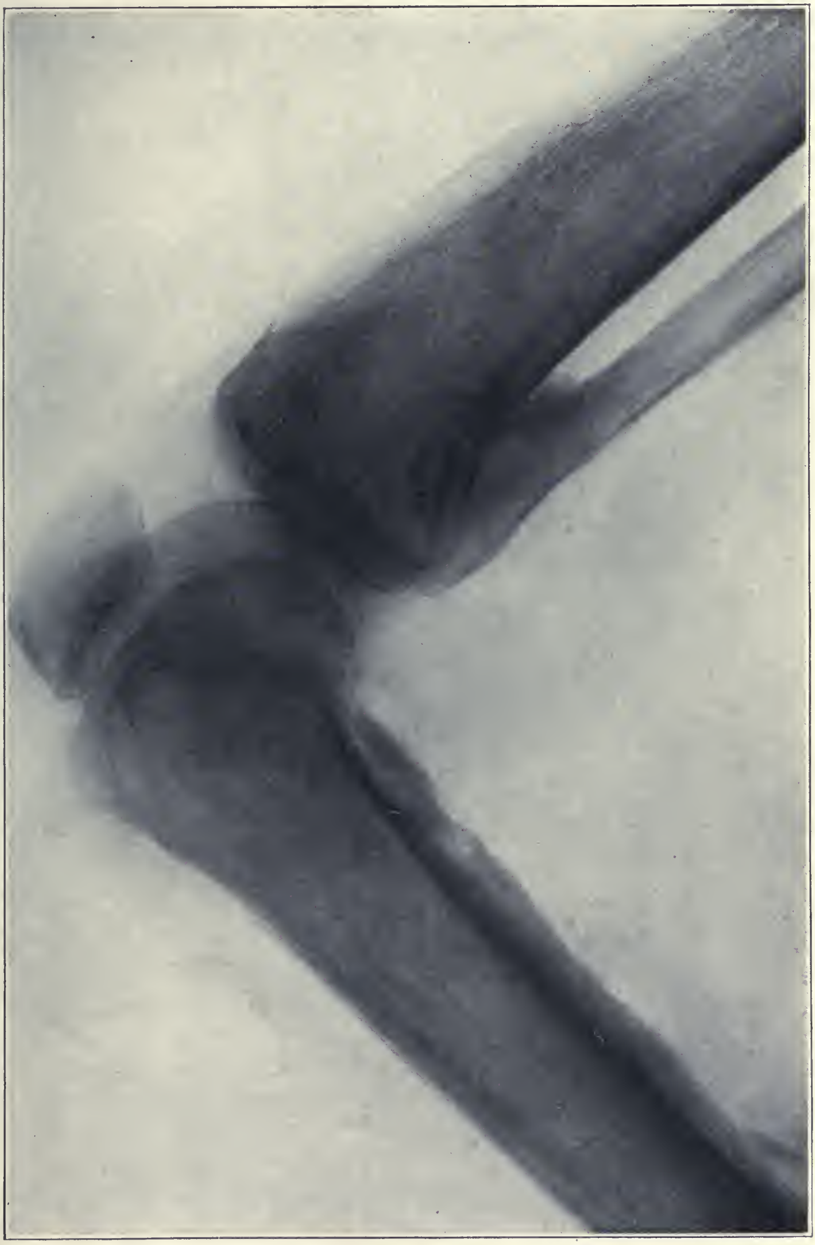

Fig. 55.—Syphilitic periostitis is usually characteristic, although it may be simulated by tuberculosis in rare instances.

from using local application for a day or two and then reexamine. In the second place this instrument affords much the best chance of showing the organisms, for if they are in the serum they cannot be missed, provided that the observer is a trained one. It must always be remembered that in the mouth there are spirochetes that closely resemble the organism of syphilis, and as a result the findings of apparent treponemata from mouth lesions must be interpreted with the greatest reserve. Personally, I never attempt to use the dark-field for the diagnosis of mouth lesions, unless I suspect a chancre, and then I take care to secure serum from deep in the growth.

When organisms cannot be demonstrated the following procedure may be instituted: With a rather long needle of about 19 gauge an enlarged neighboring lymph node is punctured and a drop or two of fluid from this is drawn up into the syringe. This is then examined by means of the dark-field. An additional refinement is the injection of one or two drops of a sterile normal saline solution into the lymph node and the withdrawal of this fluid.

Any man who attempts to diagnose a venereal sore without the aid of dark-field illumination is not only practicing medicine badly, but is morally guilty of malpractice.

DEMONSTRATION OF ORGANISMS BY STAINS

A number of stains have been recommended from time to time, the most important of these are India-ink, collargol, the Giemsa stain, the Goldhorn stain, the Romanowsky stains, and lastly the Fontana stain.

The India-ink method has fallen into disfavor because many of the inks show spiral organism that resemble the treponema. The collargol method has never proved popular. The Giemsa and Goldhorn methods are both difficult to perform. The Romanowsky stains often fail to demonstrate organisms. The Fontana or the Fontana-Tribondeau method has recently been described by Fluentes (Arch. of Dermat. and Syphil., 1921, iv, 448). The author recommends the following method. The reagents employed are: glacial, acetic acid, 1 c.c., formaldehyde, 2 c.c., and distilled water, 100 c.c.; tannin, 5 per cent, 100 c.c.; silver nitrate, 100 c.c.; pure ammonia, 10 c.c., a slide containing serum from a chancre is immersed two or three times in the first solution; it is then washed in distilled water, which is then treated for thirty seconds with the tannin solution, which has been heated until it smokes and then washed in distilled water. Lastly it is immersed in a cold silver nitrate and ammonia reagent and again washed in distilled water.

However, it should always be remembered that the use of the dark-field illuminator is much more satisfactory than that of any of the stains.

ANIMAL INOCULATION

Animal inoculation plays an important part in the diagnosis of tuberculosis, but this is not true of syphilis. The work of Engmann and Eberson (Arch. of Dermat. and Syphil., 1921, vol. iii, page 347) would seem to indicate that in certain instances the injection of serum from a suspect into the testicles of a rabbit may have some diagnostic value. If the theory of strains is finally proved it may be necessary to determine with what strain a person is affected and apparently this can be done only by animal inoculation.

LEVADITI STAIN

The use of the Levaditi stain has demonstrated organisms in the tissues in many cases. However, it is more than possible that artefacts, probably connective tissue fibrils, have confused the observer in many instances. Warthin has published (Warthin and Starry, Jour. Amer. Med. Assn., 1921, lxxvi, 234) a new method which is claimed to make it possible to demonstrate organisms within forty-eight hours. However, in one of the best equipped laboratories in the country this method has proved a flat failure. It is to be hoped that the method can be made practical for all laboratory work, for it would be a great diagnostic boon to remove a bit of suspected tissue and find the treponemata within three days. At the present time the method cannot be recommended for general use.

HISTOLOGICAL EXAMINATION

The histological examination of suspicious tissue, examined by a pathologist who *knows* the pathology of syphilis will give a correct diagnosis of syphilis in many instances. Unfortunately however, there are comparatively few pathologists who know syphilis when they see it. A panarteritis or phlebitis with a coatsleeve infiltration

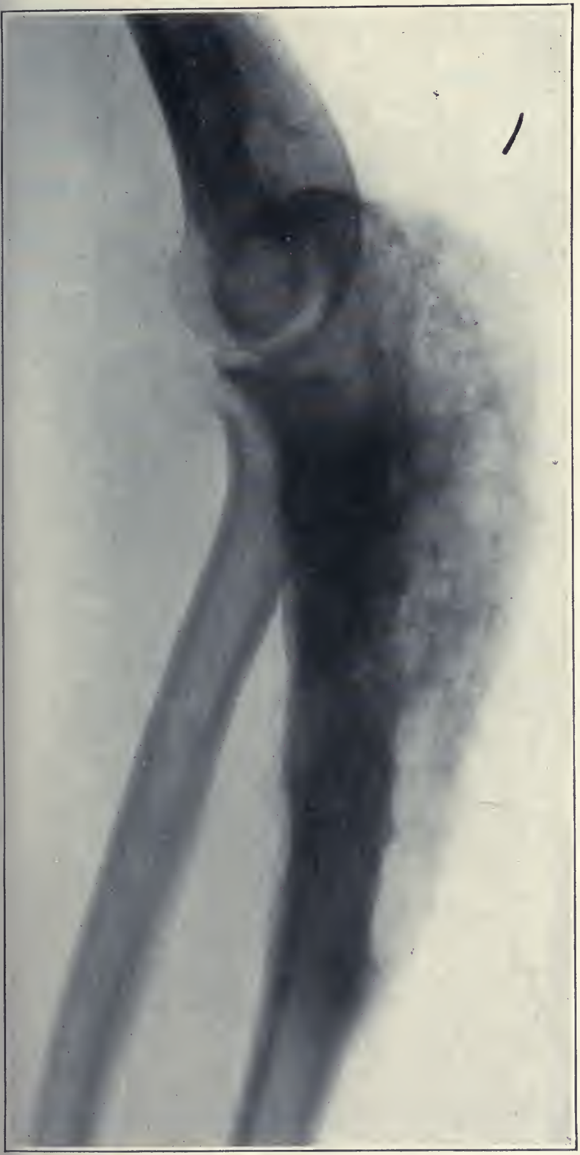

Fig. 56.—A young girl fell from a chair to the floor; within a few weeks a large swelling developed just below the elbow, which was at first thought by the surgeons to be sarcomatous, but the Roentgen rays showed periostitis, which was definitely syphilitic in character.

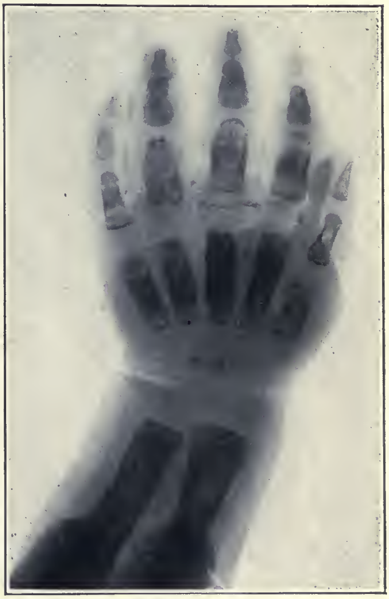

Fig. 57.—This illustration portrays the syphilis of the bones of the hands and fingers in a young child suffering from congenital syphilis.

of lymphocytes, plasma cells and fixed tissue cells is almost pathognomonic of syphilis. The illustrations will describe this point much better than mere words.

That this test is of actual value may be proved from a recent experience in the office of the author. A young physician came in with a suspicious looking rash, but without any other signs of syphilis, although a very careful physical examination was made. Blood was split in four ways and sent to four Wassermann laboratories. Two were absolutely negative, and two partially positive. One of the lesions was excised and stained with Hematoxlyn and eosin, typical syphilitic changes were found, and treatment immediately begun. At the time of the second injection of arsphenamine his blood was completely positive in several laboratories. Histologic examination of the umbilical cord forms one of the best methods for the early diagnosis of congenital syphilis. Histologic examination of the placenta will often reveal enlarged club-shaped chorionic villi. The blood vessels likewise show characteristic changes.

ROENTGEN RAY EXAMINATION

Probably the roentgen rays are of more value in determining the presence of obscure syphilis in certain organs than they are in making a general diagnosis of syphilis. And yet more than one case has been picked up by the radiologist. In the vast majority of instances this is due to the recognition of an aneurysm or of a syphilitic periostitis. The recent work of Shipley, Pearson, Welch and Green (Bulletin of Johns Hopkins Hopsital, 1921, xxxvi, page 75) indicates that congenital syphilis can frequently be diagnosed by changes in the epiphyseal line.

The x-ray will usually serve to differentiate a syphilitic process of the bone from tuberculosis, sarcoma, bone cyst, giant celled sarcoma, rickets, and injuries. One of the greatest triumphs has been the early detection of aneurysm and dilatation of the aorta. The methods of this examination are so well known that further discussion is not needed.

Most radiologists admit that it is difficult for them to distinguish syphilitic lesions of the lungs, for they believe that the shadows cast are not pathognomonic. Watkins has made a study of the condition and has reached the following conclusions: Syphilis tends to invade the lower and middle lobes, it tends to involve the tissues at the hilum first, so that the densest shadow is there, and the shadows do not bear a distinct relation to the bronchi, as in tuberculosis. At the edges they have a ragged, worm-eaten appearance. In other instances the lung is evenly speckled, or there are lance-like radiations of dense fibrous tissue. With the majority of these conclusions we are prepared to agree, although we should also like to mention still another variety, where there is a very dense shadow through the mediastinum and in the adjoining portions of the lungs. The following conditions must be differentiated: cancer, which gives a localized shadow with a sharp margin, except in the case of some infiltrating carcinomata, which cannot be distinguished; pneumokoniosis, which presents great difficulty in diagnosis; unresolved pneumonia, which is likewise difficult to distinguish; tuberculosis, which tends to first invade the upper lobes or apices and which shows distinct shadows in relation to the bronchial tree.

There are four types of gastric syphilis: syphilitic gastritis, ulcer, tumor and diffuse infiltration. The first named condition casts no shadow, so need not be considered. Many syphilitic ulcers cannot be distinguished from peptic ulcers, but in a fair number of instances one of the following findings will make the operator suspicious; multiplicity of ulcers, or absence of niche, accessory pocket or typical incisura. However, we should caution against making a positive diagnosis on the x-ray findings alone; they are simply valuable confirmatory signs. Tumors are hardly characteristic except in one particular: it is unusual for a patient with a large cancer to be in as good physical condition as are the majority of patients with hypertrophic leutic lesions. Diffuse syphilitic infiltration cannot be distinguished from a diffuse fibrosis due to other causes.

In the intestines the same syphilitic processes may occur as in the stomach. The literature is surprisingly silent as to the x-ray findings. It would seem that multiplicity of ulcers might make one suspicious. Mortimer has reported a case of syphilis of the duodenum.

THERAPEUTIC TESTS

Even at the present time there is occasional necessity to resort to the therapeutic test in order to establish a satisfactory diagnosis. This is especially true in suspected malignancy developing upon a syphilitic tongue, but may likewise be true in differentiating be-

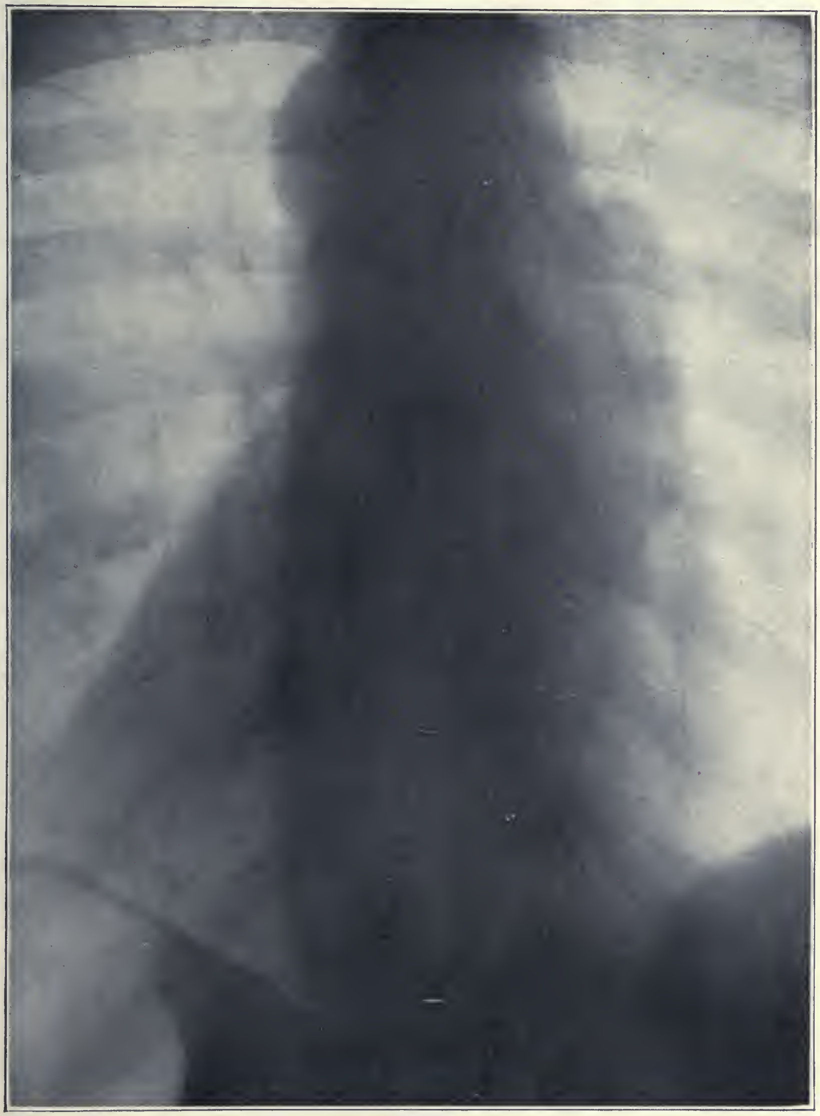

Fig. 58.—Even small aneurysms cast a definite shadow. This is one of the descending arch.

tween carcinoma and syphilis of certain viscera. Where malignancy is suspected injections or arsphenamine should be given twice a week and if a satisfactory change does not occur within three weeks it is generally safe to assume that the condition is not syphilis.

OPERATION

At times an operation may be necessary to decide between syphilis and some other tumor of certain of the viscera. Certainly, however, a chancre of the lip should be diagnosed before the operating table is reached.

AUTOPSY

Autopsy is the last word on diagnosis. Again, attention should be directed to the fact that to the naked eye appearances may be deceiving and that frequently histological examination of removed organs will reveal an unsuspected syphilis.

Now that the various methods of diagnosis have been described it may be well to classify them. The methods which will give an absolute diagnosis of syphilis are the following:

1. The appearance of certain cutaneous manifestations.
2. Perforation of the palate.
3. The recognition of interstitial keratitis.
4. Clinical signs of tabes or paresis.
5. Two reliable completely positive Wassermann reactions.
6. Positive findings in the spinal fluid.
7. Positive dark-field examination.
8. Roentgen ray examinations revealing aneurysms or syphilitic periostitis.
9. The finding of syphilitic changes at autopsy.

None of the other methods of diagnosis are infallible, although many of them are extremely suggestive and the coexistence of any two or three of them may make a diagnosis of syphilis justifiable.

The diagnosis of chancre is usually conceded to be a laboratory procedure. The reason for this is that many chancres are absolutely atypical in appearance. Practically any genital sore should be suspected of being syphilitic and this disease ruled out before the patient is discharged. It should always be recalled that it is not unusual for a chancre and a chancroid to coexist, and hence every chancroid should be regarded with utmost suspicion, for it is extremely embarrassing to cure a chancroid and have the patient return with syphilis a few weeks later.

The most valuable single diagnostic method in chancre is the dark-field examination. If antiseptics have previously been used upon the lesion this may have to be repeated daily for as much as a week, or puncture of the lymph nodes done.

The Wassermann reaction is also of considerable value. As already indicated it is not unusual for the Wassermann to become positive by the end of the second week. Where dark-field examination fails the Wassermann follow-up system may be used. By this is meant the testing of the patient's blood every four or five days during a period of at least six weeks.

Another valuable laboratory test is the excision of the chancre and the staining of it with hematoxlyn and eosin.

There is one type of chancre that is clinically characteristic. This is the large, indurated lesion that appears in the corona, feels like an oval area of cartilage nearly three-fourths of an inch in its long axis. The genital sores of scabies can usually be differentiated clinically by the finding of the disease in other portions of the body. Typical multiple patches of herpes can also be diagnosed without difficulty, although it should be remembered that in rare instances a chancre can closely simulate an herpetic lesion.

Diagnosis of secondary syphilis is usually easy. The Wassermann reaction is almost invariably positive, and there are usually enough clinical signs to enable one to make a diagnosis even without a blood examination. An examination of the skin, mucous membranes, eyes, lymph nodes and nervous system is imperative.

It is in the late stages of syphilis that diagnostic acumen is most often tested to the limit, and every procedure that has been mentioned in the preceding pages may have to be used. It should be emphasized again that the Wassermann reaction is frequently negative in the late stages of syphilis.

Section 20

PROGNOSIS OF SYPHILIS

Many clinicians feel that if a syphilitic will put himself into the hands of his physician and obey instructions he is not apt to have any further serious trouble. The pathologists do not always take this view; Warthin believes that syphilis is never cured. The new work upon syphilis of the central nervous system has caused all thoughtful clinicians to pause and consider and very few syphilologists are as optimistic as they once were.

It is probable that syphilis causes over 60,000 deaths a year in the United States. The various insurance statistics show that the average syphilitic has a mortality of 33 per cent above expectations. The author has recently reviewed his private cases of syphilis and has found that out of 230 cases which were treated some years ago, 14 are dead, 6 directly from syphilis, 4 indirectly from syphilis, and 4 from intercurrent disease.

Taken all in all, the prognosis of syphilis in any individual case is doubtful, but naturally is much better in those who do not have involvement of the central nervous system.

Serious lesions of the heart or aorta naturally make poor risks of the patient. Paresis is practically always fatal, and certain other types of neurosyphilis may end disastrously.

When a patient in the early stages of syphilis is thoroughly treated for eighteen months, and has a negative spinal fluid, the chances seem to be that he will have no further trouble if he keeps himself under observation. He may, of course, require further treatment, but in the vast majority of instances this will be the most serious inconvenience that he will suffer.

Section 21

PROPHYLAXIS

We have at our disposal complete data as to the prevention of syphilis, and it should be easily controlled were it not so intimately connected with the social problem. The sexual instinct, next to hunger, is the strongest that man possesses and it is impossible to prevent illicit sexual intercourse. The great majority of persons also object to any regulations that might control their sexual habits. Lastly, once a person has syphilis he is naturally secretive about it. No matter how unpleasant these facts may be to the reformer, or to the sanitary officer, if he is honest, he must admit them. And yet there is much that we can do to prevent the spread of syphilis and this is conceded to be necessary.

The following outline will show the various means of attack:

1. Legislation—
    - A. Notification.
    - B. Segregation.
    - C. Punishment for willful transmission.
    - D. The Surgeon General's Bill.
    - E. Control of Prostitutes.
    - F. Abolishment of Red Light District.
    - G. Control of Charlatans.
    - H. Control of Liquor.
    - I. Suitable Marriage Certificates.

2. Public Health Measures—
    - A. Better Housing.
    - B. Recreation Facilities.
    - C. Clean Books and Magazines.
    - D. Clean Plays and Movies.
    - E. Modest Dress.
    - F. Opportunities for Unfortunate Women.
    - G. Suitable Infants' Homes.

3. Education—
    - A. Physicians—
        - (a) Medical Students.
        - (b) Postgraduate Schools.
        - (c) Public Health Institutes.
        - (d) Correspondence Courses.
        - (e) Books and Journals.
    - B. Adults—
        - (a) Community Gatherings, Utilizing Churches, Clubs, Schools, Community Centres and Industrial Plants.
        - (b) Street Advertisements.
        - (c) Books and Magazines.
    - C. Children—
        - (a) School.
        - (b) Parents.
        - (c) Churches.

4. Personal Prophylaxis—
    - A. Continence.
    - B. Personal Preventive Measures, such as Condoms, Ointments, douches, soap and water.

    C. Prevention Stations.
    D. Circumcision.
    E. Arsphenamine.
    F. Vaccines.
    G. Marriage and Syphilis.
    H. Hygiene of the Syphilitic.

5. Shortening the Contagious Period—
    A. Proper Private Care.
    B. Proper Dispensaries.
    C. Proper Hospital Facilities.

LEGISLATION

While it must be admitted that no law can be enforced for which the people are not ripe, still legislation can do much good.

Notification.—There has been much discussion regarding the advisability of reporting cases, but the question has been practically settled by the happy compromise of reporting them to the local Health Department by number and not by name. However, nearly all of the states in the Union have adopted the law that should a syphilitic refuse to continue treatment, or indulge in practices liable to be injurious to the Public Health, the name must be reported. It should always be remembered that children suffering from congenital syphilis are especially difficult to trace, as the parents of such children are only too frequently careless, ignorant, or worse. We must have means to force such parents to give the children a square deal.

Segregation.—It is impossible to segregate all syphilitic patients. There are too many syphilitics, and too many in high places. In other words, to be effective, segregation might require long detention and this would seriously handicap economically any community that tried it. And most important of all, citizens would not stand for such a law. However, there can be no objection to segregating those persons having actively contagious syphilis who persist in practices apt to spread the disease; this, of course, applies chiefly to prostitutes.

Punishment for Willful Transmission.—There can be no doubt but that some syphilitic individuals will deliberately expose others. In some instances this is done simply because of lack of moral decency. In other cases the victim is determined to make others suffer. I have known of two instances where a man deliberately infected his wife and later bragged concerning it. There can be no doubt but that such persons should be severely punished.

Surgeon General's Bill.—Since the War practically all of the states have adopted laws based upon a model law drafted by the Surgeon General of the Army, Navy and Public Health Service, a law really derived from the West Australia Act. These laws provide that every case of syphilis be reported to the Health Authorities by number, not by name, but if the patient discontinues treatment, or by his acts endangers others, his name must be reported to the Health Authorities, who then assume charge and responsibility of the case. In certain states the health officers are given permission to examine any persons reasonably suspected of suffering from venereal disease and to segregate such a case should necessity arise. This provision of the law has met with marked opposition in some communities, but so far as I am aware no hardship has ever arisen because of it. As a matter of fact it is one of the real teeth of any effective regulation. The sale of patent preparations is prohibited and druggists are forbidden from prescribing over the counter. Persons suffering from syphilis are not allowed to engage in the handling of food or in other occupations which may endanger the public.

In commenting upon this law it may be said that it should always be enforced by the health authorities rather than by the police, for since time immemorial the police have either formed financial connections with the prostitutes, or have deliberately victimized them.

Control of Prostitutes.—It should be clearly understood that clandestine prostitution is far and away the largest class. A comparatively small percentage of venereal disease is acquired in houses of prostitution. Furnier believes very strongly that a prostitute with active syphilitic lesions should not be allowed to ply her trade, and most of us would agree with him that such an individual should be segregated. State regulations may be opposed upon the following grounds: first, medical supervision has always proven incomplete and unsatisfactory and it has been difficult to find suitable physicians to make examinations; second, state regulation is contrary to the constitution of the government which forbids pandering; third, a false sense of security is given the frequenter of these resorts. However, the police can stop street soliciting and to some extent the use of hotels and road houses as houses of assignation. Fortunately it is universally conceded that the state control of prostitution is by no means an important factor in combating the disease.

Abolishment of Red Light Districts.—Apparently the chief objection in the closing of the houses of prostitution is to remove temptation from the minds of men and to make illicit sexual intercourse rather more difficult and a bit unsafe from the legal aspect. However, the law of supply and demand always provides a quite sufficient number of unfortunate women who are willing to sacrifice their bodies for a few dollars. As a consequence prostitutes have simply moved from the established houses into various apartments or into some of the hotels, not always the poorest. As fast as the prostitute is chased out of one place she reappears in another and while my own beliefs are doubtless somewhat heterodox, still I am profoundly skeptical whether the great hue and cry after the prostitute has really been of any practical value. Practically every young man knows where he can find a suitable companion. In the smaller towns, however, the closing of houses has proved a real aid.

Control of Charlatans.—Venereal disease has been much treated by advertising specialists and by druggists who prescribe some nostrum. Of course, a patient treated in this way has very little chance. The laws passed by the various states and already referred to have done much to lessen this nuisance.

Control of Liquor.—It is generally recognized that the sale of alcoholics, at least too much alcohol, is intimately connected with the general sex question. Many cases of syphilis are contracted by those under the influence of liquor. When prohibition was introduced into the United States all of us wondered just what the effect would be upon the frequency of venereal disease. Owing to the fact that liquor can still be obtained with very little difficulty it is quite natural that there has been no effect whatever.

Suitable Marriage Certificates.—Certain of the western states have required that parties about to contract marriage should produce a certificate showing freedom from venereal disease. Legally this law has been a complete failure, but it has stimulated a greater interest among young persons and has unquestionably been an educational success.

PUBLIC HEALTH MEASURES

Better Housing.—Clean homes, opportunities to entertain company at home and less overcrowding are all helpful in preventing young women from going astray.

Recreation Facilities.—Suitable recreation unquestionably will help to keep the mind off of sex subjects and it is generally believed to be of importance. During the war practically all of those interested in preventing venereal disease in the army were agreed in featuring recreation as being highly beneficial.

Clean Books and Magazines.—There is no necessity for the important part that sex problems play in so much of our literature. A clean discussion of the whole sex question is infinitely superior to the stuff circulated in many of the best sellers.

Clean Plays and Movies.—The statement just made likewise applies to many of the productions seen on both the legitimate stage and on the screen.

Dress.—Unquestionably many women who make display of their personal charms consider that they are perfectly moral and modest, but they fail to realize that many men fail to take this view of the situation. However, when one remembers that the campaign to stop the wearing of furs and aigrettes on the ground of cruelty to the animals and birds was a total failure, it is difficult to see how we are going to prevent woman from blindly following the Paris fashions which are only too frequently originated by and for an extremely immoral class of women.

Opportunities for Unfortunate Women.—The education along industrial lines of fallen women has been stressed by various speakers. There can be no doubt but that women who desire to lead better lives should have every opportunity offered them, and practical steps in this direction have been singularly lacking. This is hardly to the credit of the church and various philanthropic organizations. However, it must always be remembered that a high percentage of professional prostitutes are undeveloped mentally and any attempts at educating them must be made with this fact in mind. At the present time we have no statistics as to what has been accomplished.

Suitable Infants' Homes.—There must, of course, be proper orphanages where either bona fide orphans or the children of unmarried mothers can receive proper care and these should be under suitable medical supervision. Every inmate should be examined for congenital syphilis, for the percentage of syphilis in children of this type is high. No one should adopt a child from one of these homes without having this disease ruled out.

EDUCATION

Education of Physicians.—The education of physicians regarding the recognition and treatment of venereal disease must necessarily begin in the medical schools. Fortunately this is now recognized and a full report has been made by the Committee on Medical Education. If the measures adopted in this report are lived up to by the various schools the recent graduates will have a very fair idea of the principles involved in handling syphilis.

Various postgraduate schools give the graduate a chance to better himself for the handling of venereal cases.

Public Health Institutes are yearly held in the majority of states. They have aroused a widespread general interest and have undoubtedly accomplished much good.

Under the auspices of the United States Public Health a correspondence course has been started so that physicians can refer their practical problems and secure an unbiased answer.

There are plenty of books and journals the reading of which will benefit any man seeking information.

Education—Adults.—Practical talks have been given to the adult laity by utilizing churches, clubs of all kinds, colleges, community centres, and various industrial plants. Speakers for these occasions are furnished by the local Social Hygiene Organizations or through a local Bureau of Hygiene. It has been found comparatively easy to interest the community and the attendance at meetings has steadily grown.

Various types of street and public advertisements concerning venereal disease have been tried. The Public Health Service has put placards in the men's toilets of all railroad cars. Toilets in the hotels and other semipublic places have been placarded by the local Board of Health. The central Bureau of Social Hygiene has a number of public traveling automobiles which contain exhibits. Pictures are cast upon the screen in vacant business properties.

Pamphlets and books have been published by private authors, by the U. S. Public Health Service, by the Bureau of Social Hygiene and by various local Boards of Health. The American Medical Association also has a series of pamphlets. Many of the monthly magazines have contained a remarkedly free discussion of the sex and venereal problem.

All told the average adult must have experienced considerable difficulty in escaping from a more or less liberal education as to the prevalence and dangers of venereal disease.

Education of Children.—Much stress has been placed upon teaching a certain amount of sex physiology to children. It is generally believed that this is best done through a graded and systematic course in the biology of life, first explaining the development of flowers, then of birds and then of mammals. As to just what the results will be it is too early to prognosticate. It is barely possible that a too free discussion of the sex problem may simply whet their appetites. It must also be remembered that the average child begins to acquire some sex knowledge by the time he is 10 years of age and that by the time he is 14 he has usually received a rather vicious supply of it, usually from older boys. Hence it becomes apparent that if we are to accomplish anything with children we must begin at a tender age. Of course, the ideal way is to have parents do this teaching, but a large percentage of parents are totally unfitted for it and hence the burden naturally falls upon the schools. Churches have been utilized to some extent, but the results have not been satisfactory.

PERSONAL PROPHYLAXIS

Continence.—Practically every physician now knows that continence is absolutely compatible with good health. There is no particular reason why more men should not school themselves to practice this admirable virtue, difficult though it may be to many of them. Unquestionably there is a feeling of satisfaction to be derived from a clean life that can be obtained in almost no other way. Unquestionably too, any one who takes sexual chances is indeed taking grave risks of acquiring a serious disease that will prove most unfair to his wife and children. But continence has never been practiced by all men and judging from present indications it never will be.

Personal Preventive Measures.—Condoms, that is rubber protective devices for the male organs are probably the most effective devices against acquiring or transmitting venereal diseases, but they do not protect against the risk of extragenital infection, and they have been known to break at most inopportune times. The use of a mercurial ointment following intercourse will prevent many cases of syphilis, and likewise an intraurethral injection of argyrol will usually prevent the acquiring of gonorrhea. This treatment was in general use during the war and the results were excellent when treatment could be done within eight hours of exposure and when it was given by a skilled attendant. The sale of preventive packets, as practiced in Pennsylvania, is to be deplored, for the average individual must know just how to best treat himself and such knowledge is rare. Women can use antiseptic douches with fair success. The demonstration by Reasoner that soap would almost instantly kill the causal organism of syphilis is important. The most ultramoral faddist who believes that a venereal disease is a moral policeman, can hardly raise objection to a man's washing himself with soap and water. In addition, it is a great comfort for a physician or a nurse to know that he can easily disinfect his hands in this simple way.

Prevention Stations.—During the war prevention stations were generally used by the army. They were usually in charge of a noncommissioned officer who had been given instructions in the proper methods of urethral irrigation and the applicatian of a mercurial ointment. Soldiers were forced to take treatment after exposure, and the penalties for not doing so were strictly enforced. Where the stations were efficiently managed and where the men reported promptly the results were good. At the present time there is considerable discussion as to having these stations in all large cities. Unfortunately a number of religious women's organizations are bitterly opposed to them and these silly women threaten to block any appropriation for the general venereal disease campaign if any of the appropriation goes for the maintenance of such stations. It would be hard for some of us to sympathize with one of these women should she acquire a venereal disease.

Circumcision.—This procedure has been supposed to lessen the risk of contagion, but its results are extremely doubtful.

Arsphenamine Injections.—Of late there has been considerable literature anent the possibility of aborting syphilis by the intravenous use of arsphenamine within a few hours of exposure. Various persons and animals have been inoculated with syphilis, two to five intravenous injections of arsphenamine given, and the observation made that the inoculation did not take. A final decision has not as yet been reached regarding the practicability of this method.

Vaccines.—There is no known vaccine that will prevent this disease.

Syphilis and Marriage.—There are two good reasons for not granting hasty permissions to a syphilitic to marry: first, because he is not a good life insurance risk, and the family may be deprived of its bread winner, and second, because the wife and children may contract the disease, not a pleasant thing to have happen. The recent demonstration by Engman that many syphilitics have infectious semen naturally makes one still more cautious in granting this permission.

The syphilitic woman is more apt to infect her husband when she has active lesions, but it must be remembered that treponemata have been found in the menstrual and leucorrheal discharges of women who showed no active lesion. Certain deductions are obvious: no syphilitic should marry until he has been asymptomatic and Wassermann free for at least two years since the last treatment. No patient who is reasonably suspected of having cerebrospinal syphilis should marry.

A syphilitic woman should not bear children until she has been asymptomatic and Wassermann free for at least one year and she should be carefully watched during the period of pregnancy.

Hygiene of the Syphilitic.—The syphilitic must abstain from certain things which are dangerous to his associates. Fortunately the use of arsphenamine will usually destroy all free floating parasites within a week, at least for the time being. While there are active lesions the patient must abstain from sexual intercourse and from kissing. Separate dishes and separate linen should be used during this period and he should sleep alone. He should not loan his razor, or any article that goes in the mouth to others.

SHORTENING THE CONTAGIOUS PERIOD

One of the most practical ways to lessen the prevalence of syphilis is to shorten the contagious period. As has already been pointed out this can readily be done by the use of arsphenamine.

Proper Private Care.—The majority of patients who go to a private physician do not receive proper treatment. The majority of them do not get the number of arsphenamine injections that they should have and only a few have spinal punctures done. Unfortunately there are many physicians who will give only two or three injections of arsphenamine and will charge so much for these that the patient cannot afford to go on with treatment. Such action upon the part of the physician is an outrage upon both patient and society at large. Every patient who consults a physician should arrange to see that he will receive at least a minimum amount of treatment.

Proper Dispensaries.—From the public health standpoint it is necessary that there be efficient dispensaries for the treatment of venereal diseases. Many such exist. They may be run by the U. S. Public Health Service, by the State Board of Health, by a local board of health, in conjunction with hospitals and medical schools, or exceptionally by private individuals.

In running a dispensary certain requirements are necessary. They are, first, suitable rooms which are easy of access to the patient. Second, suitable hours; this may demand night hours. Third, there should be a complete personnel. There can be no question but that the men who are working in the clinics should be paid. A salary of from fifty to seventy-five dollars a month is usually essential, although it may be necessary to pay more in case much time is demanded. Fourth, the physicians must absolutely be on time and be reasonably prompt in seeing patients. Fifth, the patient must be made to feel that an interest is taken in him. Sixth, a competent follow-up system is absolutely requisite. Seventh, there must be some arrangement in force whereby arsphenamine can be administered to the indigent. Eighth, there should be a sufficient number of beds to confine infectious cases and to do intraspinal work. Ninth, the patient should be furnished with literature apprising them of the seriousness of their disease.

Proper Hospital Facilities.—It is absolutely necessary to hospitalize some syphilitics. There are certain patients who need careful study, there are others who must have spinal punctures done, some are much better given arsphenamine in the hospital than as ambulatory patients and lastly, certain infectious cases need isolation. Every dispensary should be associated with some hospital and the dispensary physician should have ward services. It is only in this way that the best results can be secured.

QUANTITATIVE STUDIES IN SYPHILIS FROM A CLINICAL AND BIOLOGICAL POINT OF VIEW

V. Arsenic Content of the Blood and Spinal Fluid after Neo-Salvarsan in the Swift-Ellis Method of Treatment

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THE arsenic findings in the serum, clot and cerebrospinal fluid of patients treated with neo-salvarsan by the Swift-Ellis method of intraspinal therapy are recorded in this paper. Twenty-seven patients with various types of neurosyphilis were investigated and 48 sera, 49 clots and 56 spinal fluids analyzed.

The procedure of treatment was as follows: The neo-salvarsan was prepared by dissolving 0.9 gm. in 100 or 120 c.c. of sterile 0.4 per cent saline solution, prepared from chemically pure sodium chloride and injected by the gravity method. At the various intervals stated in the tables 50 c.c. of blood were withdrawn and placed on ice until the following morning. It was then centrifugalized, pipetted into a sterile tube, re-centrifugalized and transferred to a third tube when it was inactivated at 55° C.

The majority of the cases were treated intraspinally from 24 to 30 hours after the intravenous injection (see chart for exact intervals). A lumbar puncture was made, 10 to 15 c.c. of spinal fluid collected for examination, and while the needle was still *in situ* a gravity apparatus of 40 c.c. capacity was attached. Spinal fluid was permitted to run into the apparatus until about three-fourths full, when the serum was slowly added and the mixture allowed to flow into the subarachnoid space.

It will be noted that the specimen of spinal fluid to be analyzed was removed before the injection of the auto-serum. The effect of the arsenic content of the latter on the total quantity of arsenic present in the spinal fluid could not be determined until the next intraspinal injection was given, as none of these patients was punctured in the interim. For instance, by referring to the first patient (A. L.) on Table I, page 1, Serial No. 1010, it will be seen that his serum removed 30 minutes after his intravenous injection on 1/14/22 showed 3.22 mg. of metallic arsenic in 100 gms. of dried specimen. This neo-salvarsanized serum was injected intraspinally on 1/16/22. Another specimen of spinal fluid was not obtained until his next intraspinal treatment on 2/13/22, when it was analyzed and found to contain 1.92 mg. of metallic arsenic per 100 gms. of dried specimen. This arsenic content then was the result of auto-serum given on 1/16/22, plus the neo-salvarsan injected intravenously on 2/11/22. This fact should be borne in mind in connection with all the cases analyzed in these studies.

In order to obtain definite details regarding the method of procedure used in this investigation it is suggested that the reader refer to the original article by the authors in the *American Journal of the Medical Sciences,* Vol. clxiv, No. 4, October, 1922, pp. 492-513. Briefly, the above method of calculation* is based upon a wide experience in expressing small quantities in which several decimal points may be involved. As a result of nitrogen, sulphur and arsenic determinations on small quantities of material it has been found better to express the results in terms of whole numbers as far as possible. To those who engage in more detailed study of biological and physiological facts it is well known that the volume of blood changes from time to time and since it is impossible to make a blood volume determination each time a specimen is obtained we must use the most tangible method available to keep these facts on a uniform basis. Therefore, evaporation of a specimen to constant weight is the only procedure which would lead to the same results for calculation. This is the method, therefore, employed and a tabulation of the total solids is given in every table included in any of these investigations. In one column will be found the moist weight of the specimen which will assist the reader in quickly establishing the size of the specimen used for this determination; in the next one is found the dry weight or total solids of the specimen. In a third column the percentage of solids is given. With these data all who are familiar with volume work can easily calculate back to figures dealing with the moist weight or to one utilizing volume alone. The same calculations apply to the serum, clot, spinal fluid, urine, milk and to viscera. A very simple illustration might serve further to elucidate these suggestions. It is known that a person may on one day excrete A grams of urea with a certain specific gravity for the urine; on the second day the same patient may excrete A/2 grams of urea. At first glance it might appear that the urea excretion on the second day was twice as great as on the preceding day, provided no other considerations had been taken into account. Further observations, however, showed that on the second day the patient excreted twice the volume of urine as that passed on the first day, therefore, the total quantity of urea excreted remained constant, a fact which would have seemed impossible had not a volume determination been made.

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*As we have had inquiries regarding the calculations which have been made on a wet and a dry basis and additional queries on the expression "arsenic in milligrams per 100 grams of specimen," it has seemed wise at this time to give the details for calculating these values.

It is well-known that the volume of spinal fluid fluctuates within small limits. This is illustrated by measuring the intracranial pressure by means of the manometer or by animal experimentation where the effect of various drugs on the formation of the spinal fluid has been studied. From these explanations it must seem clear to the reader that the only method of expressing the results on an absolutely tangible and uniform basis would be to calculate the arsenic on a dry basis. In every instance the values which are found in the column "arsenic in mgs. per 100 gm. dried specimen" are obtained by dividing the total quantity of arsenic present in the specimen by the quantity found under "dry weight" and multiplying by 100. In determining the total quantity of arsenic, standards are employed which are prepared by using a standard arsenic solution of which 1 c.c. contains 0.000,001 grams arsenic, or, 1 c.c. contains 0.001 milligrams arsenic. Then

0.001 × parts arsenic found × 100
÷ amount of specimen, either wet or dry,
= number of mg. of arsenic in 100 gm. of specimen.

This value will be either for the moist or the dry specimen, depending upon the value used for the statement "amount of specimen."

In the following histories we present the clinical, serological, and chemical data of each case in detail:

CASE 1.—Cerebrospinal syphilis. A. L., male; age 29; chancre and secondaries in 1913; for 7 years had dull aching pains in lower part of spine and in left knee.

Physical examination: Pupils irregular; unequal, very sluggish to light; deep reflexes very active; upper more so on right side; lower on left side; heart slightly enlarged, aortic second sound somewhat accentuated; blood pressure 170/94.

Serology: Blood	9/13/21	++++
	4/10/22	+
Spinal Fluid	9/13/21	Cells 37
		Globulin +++
		Wassermann ++++ to 0.1 c.c.
		Gold Sol: Luetic curve
	4/10/22	Cells 1
		Globulin faint trace
		Wassermann +++ to 0.4 c.c.
		Gold Sol: Luetic curve

Treatment: From 9/21/21—4/10/22
14 I. V. Neosalvarsans
6 Intraspinal injections
Course of mercury

Results: Pains disappeared and patient was able to continue his work as an eccentric dancer on the vaudeville stage.

Arsenic Determinations:

1/14/22	0.6 gm. Neo.	30 minutes	later	Serum	3.22	mg.
		" "	"	Clot	0.026	"
		52 hours	"	Spinal Fluid	9.30	"
2/11/22	0.6 gm. Neo.	25 minutes	later	Serum	1.27	"
		" "	"	Clot	0.	"
		50 hours	"	Spinal Fluid	1.92	"
3/11/22	0.6 gm. Neo.	31 minutes	later	Serum	8.50	"
		" "	"	Clot	0.207	"
		29 hours	"	Spinal Fluid	5.70	"
4/10/22	0.6 gm. Neo.	20 minutes	later	Serum	1.66	"
		" "	"	Clot	0.203	"
		30 hours	"	Spinal Fluid	12.0	"

CASE 2.—Cerebrospinal syphilis (left hemiplegia). B. L., male; age 29; syphilis denied; about March, 1918, developed severe pains in ears; worse at night; one month later had difficulty in concentrating and remembering; complained of fatigue; two months later awakened in morning to find left side paralyzed; was in bed 12 weeks and received syphilitic treatment from his physician. Physical examination one year later showed pupils very irregular, unequal, with sluggish light reaction more marked on left side. Slight flatten-

ing of right side of face; all deep reflexes very active especially on the left side with clonus and Babinski. Superficial reflexes more active on right side; atrophy of left upper and lower extremities; speech slow and a little thick; left leg drags; liver 2 cm. below right costal margin.

Serology: Blood	4/23/19	+
	2/6/22	Negative
Spinal Fluid	4/23/19	Cells 24
		Globulin +++
		Wassermann ++++ to 0.2 c.c.
		Gold Sol: Paretic curve
	2/6/22	Cells 3
		Globulin Faint trace
		Wassermann +++ with 2.0 c.c.
		Gold Sol: Negative

Treatment: From 4/10/19—2/6/22
10 I. V. Salvarsans
16 I. V. Neosalvarsans
24 Intraspinal injections
Several courses of mercury

Results: There have been no further attacks. Excepting slight residuals from his old hemiplegia patient is normal.

Arsenic Determinations:

2/6/22 0.6 gm. Neo.	30 minutes	later	Serum	0.	mg.
	“ “	“	Clot	0.02	“
	30 hours	“	Spinal Fluid	2.07	“

Case 3.—Paresis. C. S., male; age 53; chancre and secondaries 30 years ago; 18 months ago nervous breakdown; for past year forgetful, irritable; bladder and sexual power weak.

Physical examination: Pupils irregular, pinpoint, fixed to light; deep reflexes hyperactive; unequal on the two sides; superficial reflexes unequal; memory and judgment very poor; speech slurring; cannot repeat test phrases; tremor; nervous and irritable.

Serology: Blood	5/18/21	++++
	3/28/22	++++
Spinal Fluid	5/18/21	Cells 10
		Globulin ++++
		Wassermann ++++ to 0.1 c.c.
		Gold Sol: Paretic curve
	3/28/22	Cells 3
		Globulin ±
		Wassermann ++++ to 0.1 c.c.
		Gold Sol: Paretic curve

Treatment: From 5/21/21—3/27/22
- 16 I. V. Neosalvarsans
- 1 I. V. Silversalvarsan
- 12 Intraspinal injections
- Several courses of mercury

Results: General health improved and he gained in weight. For a time his articulation was a little better and he was less irritable but he has since grown weaker and is passing into the simple dementing form of general paresis.

Arsenic Determinations:

3/ 6/22 0.6 gm. Neo.	20 minutes	later	Serum	0.965	mg.
	" "	"	Clot	0.277	"
	30 hours	"	Spinal Fluid	5.83	"
3/27/22 0.6 gm. Neo.	35 minutes	later	Serum	6.14	"
	" "	"	Clot	0.037	"
	26 hours	"	Spinal Fluid	2.33	"

CASE 4.—Paresis. D. N., male; age 38; chancre and secondaries in 1907. In November, 1920, developed headache, irritability, insomnia and delusions; was committed to a State Hospital for 4 months where he received about 15 intravenous treatments following which he became very depressed and listless.

Physical examination: One month later showed pupils irregular, unequal, sluggish to light; left external strabismus; deep reflexes hyperactive; more so on the right side; superficial reflexes very active; patient very depressed, apathetic; delusional ideas; memory poor; speech defect.

Serology: Blood	4/30/21	++++
	3/31/22	++
Spinal Fluid	4/30/21	Cells 18 Globulin ++++ Wassermann ++++ to 0.1 c.c. Gold Sol: Paretic curve
	3/31/22	Cells 4 Globulin Faint trace Wassermann ++++ to 0.2 c.c. Gold Sol: Paretic curve

Treatment: From 4/7/21—3/30/22
- 1 I. V. Salvarsan
- 14 I. V. Neosalvarsans
- 11 Intraspinal injections
- 1 Course of mercury

Results: All symptoms gradually disappeared under treatment over a period of several months, when remission was sufficiently complete for his firm to take him back to work which he has done continuously for over a year.

Arsenic Determinations:

1/12/22 0.6 gm. Neo.	30 minutes	later	Serum	2.80	mg.
	" "	"	Clot	0.	"
	29 hours	"	Spinal Fluid	21.0	"
2/20/22 0.6 gm. Neo.	30 minutes	later	Serum	2.33	"
	" "	"	Clot	0.02	"
	29 hrs. 30 min.	"	Spinal Fluid	16.0	"
3/30/22 0.6 gm. Neo.	25 minutes	later	Serum	3.72	"
	" "	"	Clot	0.159	"
	29 hrs. 45 min.	"	Spinal Fluid	65.5	"

CASE 5.—Tabes. D. E., male; age 43; chancre in 1902 followed by secondaries. In 1915 developed sharp shooting pain in left shin, and girdle sensation with numbness on anterior part of chest; dull occipital headaches for one year.

Physical examination: Pupils irregular, unequal, sluggish to light; arm reflexes more active on right side; knee jerks weak and unequal; right tendo-achilles absent; band of anaesthesia extending from right nipple to back with small areas below left nipple and inner sides of arms. Aortic second sound slightly accentuated; B. P. 130/80.

Serology: Blood	12/12/17	Negative
	3/23/22	Negative
Spinal Fluid	12/19/17	Cells 40 Globulin ++++ Wassermann ++++ to 0.4 c.c. Gold Sol: Luetic curve
	3/23/22	Cells 3 Globulin Trace Wassermann ++++ with 2.0 c.c. Gold Sol: Luetic curve

Treatment: From 1/17/18—3/22/22
15 I. V. Salvarsans
7 I. V. Neosalvarsans
20 I. S. Injections

Results: Clinical condition improved after the first few months of treatment; headache and nervousness disappeared. Girdle sensation and numbness persisted but in a lesser degree. Suffered occasionally from pain; developed no incoordination, ataxia or other symptoms.

Arsenic Determinations:

1/17/22 0.6 gm. Neo.	30 minutes	later	Serum	5.24	mg.
	" "	"	Clot	0.055	"
	29 hr. 40 min.	"	Spinal Fluid	0.	"
2/23/22 0.6 gm. Neo.	35 minutes	later	Serum	1.41	"
	" "	"	Clot	0.513	"
	32 hr. 15 min.	"	Spinal Fluid	Trace	

3/22/22 0.6 gm. Neo.	25 minutes	later	Serum	lost	
	" "	"	Clot	2.77	"
	29 hours	"	Spinal Fluid	29.7	"

Case 6.—Cerebrospinal syphilis. F. E., male, age 40; admits chancroid 8 years ago; many attacks of gonorrhoea; for five years has suffered from severe leg pains; for past year also from severe attacks of occipital headaches.

Physical examination: Pupils unequal, irregular, Argyll-Robertson; all deep reflexes very active, greater on right side; also superficial reflexes; sensory disturbances over different areas of body.

Serology: Blood	12/ 2/21	++++
	3/30/22	++++
Spinal Fluid	12/ 2/21	Cells 5
		Globulin ++++
		Wassermann ++++ to 0.4 c.c.
		Gold Sol: Paretic curve
	3/30/22	Cells 6
		Globulin ±
		Wassermann ++++ to 0.6 c.c.
		Gold Sol: Luetic curve

Treatment: From 12/9/21 to 3/30/22
11 I. V. Neosalvarsans
5 Intraspinal injections
6 Mercury injections

Results: Physical condition markedly improved but had recurrences of pain in occiput, cervical region and legs, however much less severe and less frequent than formerly.

Arsenic Determinations:

1/26/22 0.6 gm. Neo.	25 minutes	later	Serum	34.3	mg.
	" "	"	Clot	0.0174	"
	31 hrs. 30 min.	"	Spinal Fluid	0.	"
2/ 9/22 0.6 gm. Neo.	30 minutes	later	Serum	0.56	"
	" "	"	Clot	0.167	"
	32 hours	"	Spinal Fluid	2.60	"
3/ 8/22 0.6 gm. Neo.	26 minutes	later	Serum	2.03	"
	" "	"	Clot	0.339	"
	31 hours	"	Spinal Fluid	25.1	"
3/30/22 0.6 gm. Neo.	25 minutes	later	Serum	8.57	"
	" "	"	Clot	0.096	"
	30 hours	"	Spinal Fluid	9.26	"

Case 7.—Paresis. G. E., male, age 44, chancre in 1901 followed by secondaries; in July 1918 became nervous and depressed and had crying spells; was very forgetful; had dull frontal headaches; personality changes; unable to attend to business.

Physical examination: Pupils irregular; unequal, sluggish. Deep reflexes all very active, left greater than right; superficial reflexes sluggish; speech slow and thick; memory and attention defective.

Serology: Blood	10/12/18	++++
	3/11/22	+
Spinal Fluid	10/12/18	Cells 68 Globulin ++++ Wassermann ++++ to –0.2 c.c. Gold Sol: Paretic curve
	3/11/22	Cells 5 Globulin ± Wassermann ++++ to 0.4 c.c. Gold Sol: Paretic curve

Treatment: From 10/8/18 to 3/10/22

12 I. V. Salvarsans
24 I. V. Neosalvarsans
34 Intraspinal injections
Several courses of mercury

Results: Remission has lasted for nearly 4 years during which time patient has carried on a large business. Wife reports that occasionally he has spells of forgetfulness, otherwise, she has noted no abnormality.

Arsenic Determination:

1/13/22	0.6 gm. Neo.	32 minutes	later	Serum	0.32	mg.
		‘‘ ‘‘	‘‘	Clot	lost	
		26 hrs. 45 min.	‘‘	Spinal Fluid	3.28	‘‘
3/10/22	0.6 gm. Neo.	30 minutes	later	Serum	4.90	‘‘
		‘‘ ‘‘	‘‘	Clot	0.075	‘‘
		28 hours	‘‘	Spinal Fluid	24.0	‘‘

CASE 8.—Cerebro-spinal syphilis. H. T., male, age 42, chancre in 1899 with secondaries; six years ago developed headaches, shooting pains in body, bladder and sexual weakness. Had received over 100 injections of salvarsan intravenously and several courses of mercury without reducing his positive spinal fluid to negative.

Physical examination: Pupils irregular, unequal, sluggish; patellar and ankle reflexes very active; right greater than left; other findings negative.

Serology: Blood	10/27/21	Negative
	4/18/22	Negative
Spinal Fluid	10/27/21	Cells 3 Globulin + Wassermann ++++ to 0.6 c.c. Gold Sol: Luetic curve

4/18/22	Cells 3 Globulin Faint trace Wassermann ++++ to 1.0 c.c. Gold Sol: Weak Luetic curve

Treatment: From 10/31/21 to 4/17/22
5 I. V. Neosalvarsans
5 Intraspinal injections

Results: Shooting pains diminished in severity and Wassermann of spinal fluid was reduced in strength.

Arsenic Determination:

4/ 3/22 0.6 gm. Neo.	23 minutes	later	Serum	2.96	mg.
	‘‘ ‘‘	‘‘	Clot	0.129	‘‘
	30 hours	‘‘	Spinal Fluid	1.49	‘‘
4/17/22 0.6 gm. Neo.	15 minutes	later	Serum	9.82	‘‘
	‘‘ ‘‘	‘‘	Clot	0.	‘‘
	29 hours	‘‘	Spinal Fluid	3.70	‘‘

CASE 9.—Cerebrospinal syphilis. K. L., male, age 40, syphilis denied; for one year had difficulty in walking; was nervous; depressed; his work had grown irksome and lacked interest.

Physical examination: Pupils unequal, irregular, fixed; upper deep reflexes hyperactive and unequal; left greater than right; lower very active, right greater than left; clonus and Babinski present; superficial reflexes active and equal; no sensory disturbances; gait spastic; heart moderate hypertrophy; B. P. 170/110.

Serology: Blood	1/28/20	++++
	4/19/22	Negative
Spinal Fluid	1/28/20	Cells 21 Globulin ++++ Wassermann ++++ to 0.1 c.c. Gol Sol: Paretic curve
	4/19/22	Cells 5 Globulin ± Wassermann ++++ to 1.0 c.c. Gold Sol: Luetic curve

Treatment: From 1/29/20 to 4/19/22
13 I. V. Salvarsans
7 I. V. Neosalvarsans
17 Intraspinal injections
3 Courses mercury

Results: Gained about 20 pounds in weight and was able to resume work with interest and energy; gait improved so that stiffness troubled him only after unusual fatigue, his work requiring walking many miles daily.

Arsenic Determinations:

1/13/22 0. 6 gm. Neo.	30 minutes	later	Serum	3.39	mg.
	" "	"	Clot	lost	
	28 hrs. 45 min.	"	Spinal Fluid	1.66	"
3/10/22 0. 6 gm. Neo.	30 minutes	later	Serum	11.00	"
	" "	"	Clot	0.02	"
	28 hours	"	Spinal Fluid	23. 6	"
4/19/22 0.75 gm. Neo.	21 minutes	later	Serum	7.60	"
	" "	"	Clot	0.214	"
	29 hours	"	Spinal Fluid	0.	"

Case 10.—Juvenile paresis (Pre-paretic stage?) K. E., male, age 20; no history of syphilis in parents; boy was born at full term; no rash or snuffles; was always dull and backward in school. With special tutoring succeeded in completing high school. Does mechanical work fairly well but slower than the average; has always been difficult to get along with; complains of fatigue and insomnia.

Physical examination: Pupils irregular, unequal, fixed to light; hearing on right side diminished; all deep reflexes very active especially on right side; superficial reflexes active and equal; speech slow, and hesitating; memory faulty; intelligence below average.

Serology: Blood	1/26/21	++++
	3/21/22	++++
Spinal Fluid	1/26/21	Cells 85
		Globulin ++++
		Wasserman ++++ to 0.2 c.c.
		Gold Sol: Paretic curve
	3/21/22	Cells 5
		Globulin ±
		Wassermann ++++ to 0.4 c.c.
		Gold Sol: Paretic curve

Treatment: From 1/21/21 to 3/20/22

1 I. V. Salvarsan
11 I. V. Neosalvarsans
1 I.V. Silversalvarsan
12 Intraspinal injections
2 Courses mercury

Results: The fatigue and insomnia disappeared under treatment. Father reports that boy is more active and does his shop work with greater energy than formerly. However only simple tasks can be allotted as his memory and judgment are not dependable. His disposition is still difficult.

Arsenic Determinations:

3/20/22 0.5 gm. Neo.	25 minutes	later	Serum	Lost	
	" "	"	Clot	1.59	mg.
	29 hrs. 45 min.	"	Spinal Fluid	83.6	"

CASE 11.—Paresis. M. Y., male; age 48; syphilis denied; in May, 1919, had several attacks of motor aphasia with slight numbness of right side of body, which lasted a few moments; for several months recurring attacks.

Phyical examination: Pupils irregular, unequal, sluggish to light; right side of face weaker than left; reflexes right arm greater than left; also of lower extremities; Babinski present; speech hesitating; repeats test phrases fairly well; memory fair.

Serology: Blood	1/10/20	++++
	3/21/22	++++
Spinal Fluid	1/10/20	Cells 6 Globulin ++++ Wassermann ++++ to 0.1 c.c. Gold Sol: Paretic curve
	3/21/22	Cells 3 Globulin ± Wassermann ++++ to 0.2 c.c. Gold Sol: Paretic curve

Treatment: From 1/6/20 to 3/20/22

7 I. V. Salvarsans
24 I. V. Neosalvarsans
24 Intraspinal injections
Several courses of mercury

(In addition to above had received treatment from his former physician.)

Results: The intervals between the attacks of aphasia have been lengthened and their duration has been shorter. Occasionally has temporary loss of memory. Physically continues in good condition and is able to conduct his business. He has had no grandiose ideas nor personality alterations.

Arsenic Determinations:

3/20/22 0.6 gm. Neo.	30 minutes	later	Serum	lost
	31 hours	"	Clot	0.
	" "	"	Spinal Fluid	Trace

CASE 12.—Cerebrospinal syphilis. M. L., male; age 36; chancre 12 years ago, secondaries denied; 7 years ago a nervous breakdown; complains of tinnitus, deafness, fatigue; sexual power diminished; no bladder or rectal disturbance; no incoordination; sensation normal.

Physical examination: Pupils unequal, very irregular, almost fixed to light; hearing greatly diminished on both sides; upper deep reflexes more active on right side, patellar, left more active than right; Achilles, right more active than left; abdominal superficial reflexes more active on right side.

Serology: Blood	2/20/20	+++
	3/ 1/22	Negative
Spinal Fluid	2/27/20	Cells 4
		Globulin ++++
		Wassermann ++++ to 0.4 c.c.
		Gold Sol: Luetic curve
	3/ 1/22	Cells 3
		Globulin Faint trace
		Wassermann ++++ to 1.5 c.c.
		Gold Sol: Negative

Treatment: From 2/21/20 to 2/28/22
11 I. V. Salvarsans
5 I. V. Neosalvarsans
9 Intraspinal injections
Several courses of mercury

Results: Hearing returned practically to normal; sexual power improved; health better than at any time since infection; no longer suffers from fatigue and inability to do his work.

Arsenic Determinations:

2/28/20 0.6 gm. Neo.	27 minutes	later	Serum	0.49	mg.
	" "	"	Clot	6.86	"
	29 hours	"	Spinal Fluid	12.4	mg.

Case 13.—Optic atrophy and paresis. M. A., male; age 39; infection in 1907 with secondaries; double vision in 1917; sight became poor during following year; sexual desire lost; bladder incontinence at times.

Physical examination: Argyll-Robertson pupils; partial atrophy of both optic nerves; vision reduced 20/200 in each eye; marked central scotoma; deep reflexes all present; knee jerks weak.

Serology: Blood	6/12/18	++++
	3/20/22	+
Spinal Fluid	6/12/18	Cells 42
		Globulin +++
		Wassermann ++++ to 0.2 c.c.
		Gold Sol: Paretic curve
	3/20/22	Cells 6
		Globulin +
		Wassermann ++++ to 0.4 c.c.
		Gold Sol: Paretic curve

Treatment: From 6/12/18 to 3/20/22
16 I. V. Salvarsan
20 I. V. Neosalvarsans
28 Intraspinal injections
Several courses of mercury

Results: Vision is now R. E. 15/200; L. E. 8/200; has no frank stigmata of paresis, but is apathetic, has lost his mental keenness and is slowly retrograding clinically.

Arsenic Determinations:

1/23/22 0.6 gm. Neo.	30 minutes	later	Serum	1.72	mg.
	" "	"	Clot	0.057	"
	25 hrs. 30 min	"	Spinal Fluid	3.50	"
2/ 6/22 0.6 gm. Neo.	25 minutes	later	Serum	2.17	"
	" "	"	Clot	0.005	"
	24 hrs. 15 min.	"	Spinal Fluid	3.10	"
3/20/22 0.6 gm. Neo.	25 hours	later	Serum	1.03	"
	" "	"	Clot	lost	
	29 hours	"	Spinal Fluid	2.87	"

Case 14.—Tabes and optic atrophy. R. N., male; aged 39; chancre 15 years ago followed by sore throat; in 1919 failing vision in left eye, followed by same in right eye; shooting pains; ataxia, and slowness of bladder for one year; numbness in right hand occasionally; nervousness for two years.

Physical examination: Pupils unequal, irregular, fixed; all deep and superficial reflexes absent; hypotonus; marked Rhomberg. Moderate ataxia.

Serology: Blood	8/26/21	++++
	1/31/22	++++
Spinal Fluid	8/26/21	Cells 10 Globulin +++ Wassermann ++++ to 0.2 c.c. Gold Sol: Luetic curve
	1/31/22	Cells 5 Globulin ± Wassermann ++ to 0.2 c.c. Gold Sol: Luetic curve

Treatment: From 8/17/21 to 1/30/22
- 9 I. V. Neosalvarsans
- 7 Intraspinal injections
- 1 Course of mercury

(In 1919 received 10 doses of salvarsan and 20 of mercury)

Results: Eyes remained unchanged; pains and nervousness were greatly diminished.

Arsenic Determinations:

1/30/22 0.6 gm. Neo.	40 minutes	later	Serum	1.04	mg.
	" "	"	Clot	0.206	"
	29 hours	"	Spinal Fluid	1.09	"

Case 15.—Taboparesis. R. H., male; age 32; chancre in 1906; secondaries denied; in 1910 shooting pains in legs; in 1920 developed mental symptoms.

Physical examination: Pupils irregular; unequal; Argyll-Robertson; deep reflexes lower extremities absent; upper extremities more active on right side; sexual power lost.

Serology:	Blood	10/24/14	Negative
		4/18/22	Negative
	Spinal Fluid	10:12/14	Cells 12 Globulin + Wassermann ++ with 0.6 c.c. Gold Sol test not done in 1914
		4/18/22	Cells 5 Globulin + Wassermann ++++ with 0.2 c.c. Gold Sol: Paretic curve

Treatment: From 9/4/20 to 4/17/22

1 I. V. Salvarsan
18 I. V. Neosalvarsans
7 Intraspinal injections
Several courses of mercury
(In 1916 received 6 I. V. Salvarsans)

Results: Patient was first seen in 1914 when diagnosis of tabes dorsalis was made. When seen in 1920 he presented mental symptoms and a strongly positive fluid with 30 cells; ++++ Globulin; Wassermann ++++ to 0.1 c.c. and a paretic curve. In the interim he had taken treatment in a desultory fashion. Under vigorous treatment his mental symptoms cleared for a few months when he had a relapse and slowly deteriorated for a year, developed convulsions and died.

Arsenic Determinations:

3/13/22	0.6 gm. Neo.	20 minutes	later	Serum	Lost	
		" "	"	Clot	0.331	mg.
		31 hrs. 15 min.	"	Spinal Fluid	35.08	"
3/29/22	0.6 gm. Neo.	30 minutes	later	Serum	11.0	"
		" "	"	Clot	0.411	"
		31 hours	"	Spinal Fluid	2.63	"
4/17/22	0.6 gm. Neo.	16 minutes	later	Serum	0.435	"
		" "	"	Clot	0.087	"
		28 hours	"	Spinal Fluid	4.76	"

CASE 16.—Tabes. S. R., male; age 44; chancre 1899; secondaries denied; for 15 years pains in extremities and girdle sensation. Bladder incontinent at times.

Physical examination: Pupils unequal, irregular, Argyll-Robertson; deep reflexes upper extremities active, right greater than left; of lower extremities absent; area of anesthesia below left breast; no ataxia.

Serology:	Blood	2/17/21	Doubtful
		3/28/22	Negative
	Spinal Fluid	2/17/21	Cells 20
			Globulin ++
			Wassermann ++++ to 0.2 c.c.
			Gold Sol: Luetic curve
		3/28/22	Cells 2
			Globulin ±
			Wassermann ++++ to 0.6 c.c.
			Gold Sol: Luetic curve

Treatment: From 3/4/21—3/27/22
12 I. V. Neosalvarsans
11 Intraspinal injections

(Had had numerous intravenous injections from his former physician during the previous year.)

Results: Attacks of pain have been less frequent but no less severe; bladder control and numbness in leg have improved; disease has not progressed.

Arsenic Determinations:

2/ 2/22	0.6 gm. Neo.	27 minutes	later	Serum	1.04	mg.
		" "	"	Clot	0.116	"
		29 hours	"	Spinal Fluid	5.16	"
3/27/22	0.6 gm. Neo.	35 minutes	later	Serum	1.46	"
		" "	"	Clot	0.677	"
		30 hrs. 30 min.	"	Spinal Fluid	Trace	

CASE 17.—Meningo-vasculitis. S. N., male; age 61; chancre 30 years ago followed by secondaries on skin and in mouth. About 10 years ago had a nervous breakdown which lasted two years. For several months has complained of extreme nervousness, occipital headaches, mental depression, forgetfulness, insomnia and inability to work.

Physical examination: Pupils are equal; irregular in shape, slightly sluggish; hearing diminished in both ears; all the deep reflexes are very active, equal in the upper extremities, greater on the right side in the lower extremities; abdominal and epigastric reflexes weak, cremasterics absent. B. P. 145/84.

Serology:	Blood	1/22/18	++++
		3/30/22	++++
	Spinal Fluid	1/16/18	Cells 58
			Globulin ++++
			Wassermann ++++ to 0.2 c.c.
			Gold Sol: Paretic curve
		3/30/22	Cells 2
			Globulin trace
			Wassermann ++++ to 0.8 c.c.
			Gold Sol: Luetic curve

Treatment: 1/22/18—3/30/22
- 16 I. V. Salvarsans
- 19 I. V. Neosalvarsans
- 29 Intraspinal injections
- Several courses of mercury

Results: Following each course of treatment a temporary improvement took place and he was able to carry on exacting legal work for a while; then a relapse would occur with insomnia, memory defects and depression.

Arsenic Determinations:

1/19/22	0.45 gm. Neo.	30 minutes	later	Serum	Trace	
		“ “	“	Clot	0.18	mg.
		31 hours	“	Spinal Fluid	Trace	
3/30/22	0.5 gm. Neo.	30 minutes	later	Serum	5.18	mg.
		“ “	“	Clot	0.297	“
		30 hrs. 45 min.	“	Spinal Fluid	Trace	

CASE 18.—Cerebrospinal syphilis. S. A., male, age 46; chancre 1897, secondaries denied; for ten years sexually impotent; for three years very nervous and forgetful; sleeps poorly; depressed mentally.

Physical examination: Pupils equal, slightly irregular; react to light and accommodation; upper reflexes active and equal; knee and ankle jerks very active; superficial reflexes sluggish; heart negative.

Serology:	Blood	10/31/21	++++
		4/18/22	Negative
	Spinal Fluid	10/31/21	Cells 40
			Globulin ++++
			Wassermann ++++ to 0.4 c.c.
			Gold Sol: Luetic curve
		4/18/22	Cells 2
			Globulin ±
			Wassermann ± with 2.0 c.c.
			Gold Sol: Weak luetic curve

Treatment: From 11/21/21—4/17/22
- 10 I. V. Neosalvarsans
- 7 Intraspinal injections
- 1 Course mercury

(A year previously had received two courses of salvarsan and mercury from former physician.)

Results: No change in sexual power; memory improved; nervousness less; depression disappeared; general condition better.

Arsenic Determinations:

1/17/22	0.6 gm. Neo.	31 minutes	later	Serum	8.60	mg.
		" "	"	Clot	0.031	"
		29 hrs. 30 min.	"	Spinal Fluid	0.615	"
1/31/22	0.6 gm. Neo.	37 minutes	later	Serum	7.70	"
		" "	"	Clot	0.053	"
		31 hrs. 30 min.	"	Spinal Fluid	81.9	"
3/20/22	0.6 gm. Neo.	26 minutes	later	Serum	0.	"
		" "	"	Clot	0.422	"
		31 hrs. 30 min.	"	Spinal Fluid	8.17	"
4/17/22	0.6 gm. Neo.	16 minutes	later	Serum	6.61	"
		" "	"	Clot	0.039	"
		29 hours	"	Spinal Fluid	0.	"

CASE 19.—Paresis. S. E., male, age 38; syphilis denied; wife stated that for one year she had noticed husband's memory and judgment were defective and that he acted queerly; could not concentrate and had a nervous breakdown in May 1921.

Physical examination: Pupils irregular, unequal, and fixed, deep reflexes very active; slightly unequal; speech hesitating; cannot repeat test phrases; marked tremor; memory and attention poor; character alterations.

Serology:	Blood	11/ 5/21	++++
		1/25/22	++++
	Spinal Fluid	11/ 5/21	Cells 7
			Globulin ++++
			Wassermann ++++ to 0.1 c.c.
			Gold Sol: Paretic curve
		1/25/22	Cells 3
			Globulin +
			Wassermann ++++ to 0.2 c.c.
			Gold Sol: Paretic curve

Treatment: From 11/7/21—1/25/22
9 I. V. Neosalvarsans
3 Intraspinal injections
1 Course of mercury

Results: Mental condition cleared considerably; patient showed an interest in his surroundings. Speech and memory improved so he could be sent on simple errands by himself; became tidier in his habits.

Arsenic Determinations:

1/25/22	0.6 gm. Neo.	30 minutes	later	Serum	4.50	mg.
		" "	"	Clot	0.054	"
		26 hours	"	Spinal Fluid	Trace	

CASE 20.—Cerebrospinal syphilis. S. S., male; age 44; chancre 22 years ago followed by mucus patches; for 7 or 8 years has had severe shooting pains in legs; for past year nervous, irritable, sexual power decreased.

Physical examination: Pupils unequal, irregular, sluggish; hearing diminished; deep reflexes upper extremities active and equal. Knee and ankle jerks hyperactive, left more so than right. Aortic second accentuated. Blood Pressure 176/100.

Serology:	Blood	8/16/19	++++
		3/16/22	+
	Spinal Fluid	8/16/19	Cells 31 Globulin ++++ Wassermann ++++ to 0.2 c.c. Gold Sol: Paretic curve
		3/16/22	Cells 6 Globulin ± Wassermann ++++ to 1.0 c.c. Gold Sol: Luetic curve

Treatment: From 9/6/19—3/14/22
10 I. V. Salvarsans
15 I. V. Neosalvarsans
8 Intraspinal injections
Several courses of mercury

Results: Hearing improved considerably; nervousness and irritability disappeared; sexual power increased; short attacks of pain recurred at long intervals.

Arsenic Determinations:

3/14/22 0.6 gm. Neo.	30 minutes	later	Serum	Lost	
	" "	"	Clot	0.616	mg.
	50 hours	"	Spinal Fluid	1.53	"

CASE 21.—Tabes. S. G., female; age 36; married 12 years; husband was infected before marriage; for 8 years she has had severe headaches, pain in joints, nervousness, unsteadiness in legs and gastric crises.

Physical examination: Pupils irregular, unequal, respond to light. Deep reflexes of lower extremities absent; gait unsteady, marked Rhomberg.

Serology:	Blood	2/ 4/22	Negative
		3/18/22	Negative
	Spinal Fluid	2/ 4/22	Cells 3 Globulin faint trace Wassermann +++ to 2.0 c.c. Gold Sol: Luetic curve
		3/18/22	Cells 1 Globulin ± Wassermann ± with 2.0 c.c. Gold Sol: Weak luetic curve

Treatment: From 2/4/22—3/17/22
2 I. V. Neosalvarsans
2 Intraspinal injections

Results: She had previously received a number of intravenous injections from her former physician which had lessened the severity of her symptoms. The treatments above exerted no appreciable influence on her condition.

Arsenic Determinations:

3/17/22 0.45 gm. Neo.	25 minutes	later	Serum	Lost	
	" "	"	Clot	0.041	mg.
	26 hours	"	Spinal Fluid	2.93	"

CASE 22.—Early paresis. V. N., male; age 51; chancre in 1907 with secondaries of skin; complains of irritability, mental inactivity and slow speech.

Physical examination: Pupils equal, round, sluggish to light; arm reflexes sluggish; knee and ankle jerks very active, right more so than left. Memory poor; attention and speech disturbance; hypertrophy of heart with slight mitral insufficiency; B. P. 120/76.

Serology:	Blood	12/ 2/21	++++
		3/10/22	++++
	Spinal Fluid	12/ 2/21	Cells 10 Globulin ++++ Wassermann ++++ to 0.1 c.c. Gold Sol: Paretic curve
		3/10/22	Cells 4 Globulin + Wassermann ++++ to 0.2 c.c. Gold Sol: Paretic curve

Treatment: From 11/25/21—3/10/22
11 I. V. Neosalvarsans
7 Intraspinal injections

(Had received combined treatment during previous year from former physician.)

Results: Patient after every course of treatment showed a marked improvement in his mental condition and was able to resume and conduct his business. After a rest period of two or three months or longer he would become irritable, forgetful and develop more speech difficulty. He has had one attack of aphasia and weakness of the left arm.

Arsenic Determinations:

1/20/22 0.6 gm. Neo.	30 minutes	later	Serum	13.0	mg.
	" "	"	Clot	Lost	
	32 hours	"	Spinal Fluid	0.	"
2/17/22 0.6 gm. Neo.	25 minutes	later	Serum	13.7	"
	" "	"	Clot	0.014	"
	7 hrs. 30 min.	"	Spinal Fluid	69.0	"

3/10/22 0.6 gm. Neo.	30 minutes	later	Serum	5.93	"
	" "	"	Clot	0.121	"
	30 hours	"	Spinal Fluid	74.0	"

Case 23.—Meningo-vascular syphilis. W. L., male; age 40; syphilis denied. In October, 1918, patient became extremely nervous and excited; talked loudly and slept poorly; developed grandiose ideas and became very extravagant.

Physical examination: Pupils unequal, oval, sluggish to light, slight ptosis of left lid; arm reflexes active, more so on right side. Left patellar active, right absent; both ankle jerks absent. Superficial reflexes present but unequal; state of mental exaltation.

Serology:	Blood	12/21/18	++++
		3/23/22	Negative
	Spinal Fluid	12/21/18	Cells 22
			Globulin ++++
			Wassermann ++++ to 0.2 c.c.
			Gold Sol: Paretic curve
		3/23/22	Cells 2
			Globulin very faint trace
			Wassermann Negative with 2.0 c.c.
			Gold Sol: Negative

Treatment: From 12/14/18—3/22/22
23 I. V. Salvarsans
21 I. V. Neosalvarsans
33 Intraspinal injections

Results: From his clinical and serological findings a diagnosis of paresis was made. The course of his disease, however, and the regression of all symptoms under treatment with a negative fluid, caused us to change the diagnosis from a parenchymatous to a meningo-vascular type of neurosyphilis. He is still under observation and continues normal.

Arsenic Determinations:

3/22/22 0.6 gm. Neo.	28 minutes	later	Serum	Lost	
	" "	"	Clot	0.56	mg.
	27 hours	"	Spinal Fluid	36.7	"

Case 24.—Cerebrospinal syphilis. W. T., male; age 31; chancre and secondaries in 1912; received one salvarsan treatment and mercury for one year; in 1913 and 1914 had five salvarsans; for one year has had dull headaches; for two months dizziness; feels dull mentally.

Physical examination: Pupils equal, round, slightly sluggish to light, upper reflexes and lower reflexes active and equal; hearing right side somewhat impaired.

Serology: Blood	11/ 7/18	++++
	1/13/22	Negative
Spinal Fluid	11/17/18	Cells 58 Globulin + Wassermann ++++ to 0.2 c.c. Gold Sol: Luetic curve
	1/13/22	Cells 5 Globulin ± Wassermann ++++ to 1.5 c.c. Gold Sol: Weak luetic curve

Treatment: From 10/10/18—1/12/22
22 I. V. Salvarsans
6 I. V. Neosalvarsans
23 Intraspinal injections

Results: All subjective disabilities disappeared and patient reports himself as entirely well.

Arsenic Determinations:

1/12/22	0.6 gm. Neo.	30 minutes	later	Serum	0.256 mg.
		" "	"	Clot	Lost
		28 hrs. 45 min.	"	Spinal Fluid	6.84 "

CASE 25.—Juvenile paresis (?) Meningo-vasculitis (?). W. G., female; age 13; born with syphilitic manifestations; mercury rubs for five years; when nine years old developed tremor and spastic gait.

Physical examination: Pupils dilated, unequal and fixed to light; all deep reflexes very active; Babinski and clonus; gait spastic; retarded mentally about 2 years; moody; irritable and difficult to manage; speech disturbance.

Serology: Blood	10/9/20	++++
	2/28/22	++++
Spinal Fluid	10/9/20	Cells 87 Globulin ++++ Wassermann ++++ to 0.1 c.c. Gold Sol: Paretic curve
	2/28/22	Cells 3 Globulin + Wassermann +++ to 0.1 c.c. Gold Sol: Paretic curve

Treatment: From 11/3/20–2/28/22
16 I. V. Neosalvarsans
13 Intraspinal injections
Several courses of mercury

Results: Spasticity has increased somewhat. Mentally a decided improvement has been evident to her parents and teachers; has been able to concentrate better and shows more interest in her studies; has always been interested in natural history and excels in anything connected with this subject.

Arsenic Determinations:

1/31/22	0.45 gm.	Neo.	20 minutes later	Serum	1.60 mg.
			20 minutes later	Clot	0.119 mg.
			27 hours later	Spinal Fluid	1.14 mg.
2/28/22	0.45 gm.	Neo.	20 minutes later	Serum	3.73 mg.
			20 minutes later	Clot	0.017 mg.
			26 hours later	Spinal Fluid	19.6 mg.

CASE 26.—Tabes. W. N., male; age 39; chancre in 1903 with secondaries. Three years ago complained of indigestion, nervousness, and numbness of scalp. For one month dull pain around belt line, weakness and fatigue.

Physical examination: Pupils unequal; irregular, Argyll-Robertson; arm reflexes active and equal; patellar and Achilles reflexes absent; superficial reflexes hyperactive; otherwise negative.

Serology:	Blood	1/18/21	Negative
		3/31/22	Negative
	Spinal Fluid	2/11/21	Cells 15 Globulin + Wassermann ++++ to 0.4 c.c. Gold Sol: Luetic curve
		4/1/22	Cells 4 Globulin Faint trace Wassermann ± with 2.0 c.c. Gold Sol: Negative

Treatment: From 2/11/21–3/31/22
10 I. V. Neosalvarsans
8 Intraspinal injections
2 Courses of mercury

(Had received a number of salvarsan injections from his former physician the year before.)

Results: Has been free from all subjective symptoms for one year and gained 14 pounds in weight.

Arsenic Determinations:

2/10/22	0.6	Neo.	25 minutes later	Serum	3.15 mg.
			25 minutes later	Clot	0.076 mg.
			25 hours later	Spinal Fluid	0.
3/31/22	0.6	Neo.	20 minutes later	Serum	20.5 mg.
			20 minutes later	Clot	0.405 mg.
			28 hours later	Spinal Fluid	51.4 mg.

Case 27.—Tabes. Y. P., male, age 40, chancre in 1902; secondaries denied. Ten years ago severe shooting pains over left instep, then all over body; for several years occasionally double vision; nervous and irritable for three years; bladder anesthetic for two years; sexual power poor for one year.

Physical examination: Pin point fixed pupils; all deep reflexes absent; superficial present but unequal; coordination arms and legs poor; Rhomberg; gait slightly impaired.

Serology:	Blood	6/25/21	Negative
		2/ 9/22	Negative
	Spinal Fluid	6/25/21	Cells 56
			Globulin ++
			Wassermann ++++ to 0.2 c.c.
			Gold Sol: Luetic curve
		2/ 9/22	Cells 3
			Globulin Faint Trace
			Wassermann ++++ to 0.8 c.c.
			Gold Sol: Luetic Curve

Treatment: From 7/13/21–2/7/22
10 I. V. Neosalvarsans
6 Intraspinal injections

Results: Pains became less frequent and severe; was less nervous and able to concentrate better; memory improved. Bladder and sexual power remained same; general health much better.

Arsenic Determinations:

1/9/22	0.6	Neo.	30 minutes later	Serum	Trace
			30 minutes later	Clot	Lost
			29 hrs. 40 min. later	Spinal Fluid	0.0 mg.
2/7/22	0.6	Neo.	25 minutes later	Serum	7.30 mg.
			25 minutes later	Clot	0.019 mg.
			31 hours later	Spinal Fluid	11.6 mg.

EXPLANATION OF ABBREVIATIONS USED IN TABLES:

I. V. = Intravenous injection
I. S. = Intraspinal injection
Dr. = Drainage
S. E. = Swift-Ellis method of intraspinal treatment
S. F. = Spinal Fluid
S.; Sal.; Salv. = Salvarsan
S. S. = Silver Salvarsan
Neo. = Neosalvarsan
Glob. = Globulin
Wass. = Wassermann
I = Primary Syphilis
II = Secondary Syphilis
III = Tertiary Syphilis
C. S. L. = Cerebro-spinal syphilis
G. P. = General paresis

TABLE I

COMBINATION CHART SHOWING ARSENIC CONTENT OF SPINAL FLUID, SERUM AND CLOT AFTER THE USE OF NEOSALVARSAN IN THE SWIFT-ELLIS METHOD OF TREATMENT

CASE	PATIENT	SERIAL NO.	NO. PREVIOUS I. V. INJEC.	NO. PREVIOUS I. S. INJEC.	DOSE OF DRUG	TIME AFTER INJEC.	WT. OF SPECIMEN		PER CENT SOLIDS	AS. IN MG. PER 100 GMS. DRIED SPEC.	AGE	SEX AND COLOR	SPINAL FLUID FINDINGS				BLOOD WASS.	DURATION OF INFECTION	DIAGNOSIS AND REMARKS
							MOIST	DRY					CELLS	GLOB.	WASSERMANN	GOLD SOL			
1	A. L. S. F.	1041	19 S. 10 neo	2 S. E.	0.6	52 hr.	8.0288	0.0857	1.06	9.30	29	M. W.	5	+	++++ 0.4 c.c.	1233210000	++++	9 yr.	C. S. L.; clinical manifestations.
	Serum	1010	19 S. 10 neo		0.6	30 min.	3.8483	0.4129	10.72	3.22	29	M. W.					++++	9 yr.	C. S. L.; clinical manifestations.
	Clot	1019	19 S. 10 neo		0.6	30 min.	28.8930	11.3530	39.29	0.026	29	M. W.					++++	9 yr.	C. S. L.; clinical manifestations.
1	A. L. S. F.	1263	19 S. 11 neo	3 S. E.	0.6	50 hr.	4.7962	0.0513	1.07	1.92	29	M. W.	3	+	+++ 0.4 c.c.	1233210000	++++	9 yr.	C. S. L.; clinical manifestations.
	Serum	1264	19 S. 11 neo		0.6	25 min.	2.8734	0.2761	9.61	1.27	29	M. W.					++++	9 yr.	C. S. L.; clinical manifestations.
	Clot	1280	19 S. 11 neo		0.6	25 min.	23.2134	7.9885	34.19	0	29	M. W.					++++	9 yr.	C. S. L.; clinical manifestations.
1	A. L. S. F.	1407	19 S. 12 neo	4 S. E.	0.6	29 hr.	4.9447	0.0500	1.01	5.70	29	M. W.	6	+	+++ 0.4 c.c.	1233210000	++++	9 yr.	C. S. L.; clinical manifestations.
	Serum	1408	19 S. 12 neo		0.6	31 min.	2.7730	0.2743	9.93	8.50	29	M. W.					++++	9 yr.	C. S. L.; clinical manifestations.
	Clot	1412	19 S. 12 neo		0.6	31 min.	27.0400	11.2535	41.61	0.207	29	M. W.					++++	9 yr.	C. S. L.; clinical manifestations.
1	A. L. S. F.	1704	19 S. 13 neo	5 S. E.	0.6	30 hr.	2.4186	0.0250	1.03	12.0	29	M. W.	1	Trace	+++ 0.4 c.c.	1233210000	++++	9 yr.	C. S. L.; clinical manifestations.
	Serum	1705	19 S. 13 neo		0.6	20 min.	3.8114	0.3608	9.46	1.66	29	M. W.					++++	9 yr.	C. S. L.; clinical manifestations.
	Clot	1706	19 S. 13 neo		0.6	20 min.	25.4574	9.9825	39.21	0.203	29	M. W.					++++	9 yr.	C. S. L.; clinical manifestations.
2	B. L. S. F.	1221	10 S. 15 neo	23 S. E.	0.6	30 hr.	5.0160	0.0482	0.96	2.07	26	M. W.	3	+	+++ 2.0 c.c.	1111000000	Neg.	Denied	C. S. L. (hemiplegia) spinal fluid strongly positive before treatment.
	Serum	1222	10 S. 15 neo		0.6	30 min.	3.7048	0.3495	9.43	0	26	M. W.					Neg.	Denied	C. S. L. (hemiplegia) spinal fluid strongly positive before treatment.
	Clot	1220	10 S. 15 neo		0.6	30 min.	20.6576	9.7310	47.10	0.02	26	M. W.					Neg.	Denied	C. S. L. (hemiplegia) spinal fluid strongly positive before treatment.
3	C. S. S. F.	1402	1 SS. 14 neo	10 S. E.	0.6	30 hr.	4.5725	0.0514	1.12	5.83	53	M. W.	5	++++	++++ 0.1 c.c.	5555431000	++++	32 yr.	Paresis; clinical symptoms.
	Serum	1403	1 SS. 14 neo		0.6	20 min.	3.7143	0.3453	9.29	0.965	53	M. W.					++++	32 yr.	Paresis; clinical symptoms.
	Clot	1415	1 SS. 14 neo		0.6	20 min.	25.4570	10.8225	42.51	0.277	53	M. W.					++++	32 yr.	Paresis; clinical symptoms.
3	C. S. S. F.	1569	1 SS. 15 neo	11 S. E.	0.6	26 hr.	3.9895	0.0428	1.07	2.33	53	M. W.	3	Trace	++++ 0.1 c.c.	5555431000	++++	32 yr.	Paresis; clinical symptoms.
	Serum	1570	1 SS. 15 neo		0.6	35 min.	2.2300	0.2442	10.90	6.14	53	M. W.					++++	32 yr.	Paresis; clinical symptoms.
	Clot	1571	1 SS. 15 neo		0.6	35 min.	23.9372	8.1549	34.06	0.037	53	M. W.					++++	32 yr.	Paresis; clinical symptoms.
4	D. N. S. F.	1014	1 S. 11 neo	8 S. E.	0.6	29 hr.	4.5260	0.0475	1.04	21.0	38	M. W.	4	Trace	++++ 0.2 c.c.	5555431000	++	15 yr.	Paresis; remission.
	Serum	1013	1 S. 11 neo		0.6	30 min.	4.3402	0.3970	9.14	2.80	38	M. W.					++	15 yr.	Paresis; remission.

TABLE I—Cont'd

4	D. N.	S. F.	1355	1 S. 12 neo	9 S. E.	0.6	29½ hr.	4.3498	0.0492	1.13	16.0	38	M. W.	4	Trace	++++ 0.2 c.c.	5555431000	++	15 yr.	Paresis; remission.
		Serum	1356	1 S. 12 neo		0.6	30 min.	4.9750	0.4290	8.62	2.33	38	M. W.					++	15 yr.	Paresis; remission.
		Clot	1391	1 S. 12 neo		0.6	30 min.	16.8140	5.9175	35.19	0.02	38	M. W.					++	15 yr.	Paresis; remission.
4	D. N.	S. F.	1551	1 S. 13 neo	10 S. E.	0.6	29¾ hr.	2.7074	0.0305	1.12	65.5	38	M. W.	4	Trace	++++ 0.2 c.c.	5555431000	++	15 yr.	Paresis; remission.
		Serum	1552	1 S. 13 neo		0.6	25 min.	3.6270	0.3219	8.87	3.72	38	M. W.					++	15 yr.	Paresis; remission.
		Clot	1553	1 S. 13 neo		0.6	25 min.	25.0721	10.4412	41.64	0.159	38	M. W.					++	15 yr.	Paresis; remission.
5	D. E.	S. F.	1082	15 S. 5 neo	17 S. E.	0.65	29 hrs. 40 min.	5.8669	0.0610	1.03	0	43	M. W.	2	Trace	+++ 2.0 c.c.	1111000000	Neg.	20 yr.	Tabes.
		Serum	1033	15 S. 5 neo		0.65	30 min.	3.9250	0.3426	8.72	5.24	43	M. W.					Neg.	20 yr.	Tabes.
		Clot	1034	15 S. 5 neo		0.65	30 min.	23.1507	8.9827	38.80	0.055	43	M. W.					Neg.	20 yr.	Tabes.
5	D. E.	S. F.	1357	15 S. 6 neo	18 S. E.	0.6	32¼hr.	3.2768	0.0400	1.22	Trace	43	M. W.	2	Trace	+++ 2.0 c.c.	1111000000	Neg.	20 yr.	Tabes.
		Serum	1358	15 S. 6 neo		0.6	35 min.	2.9665	0.2820	9.50	1.41	43	M. W.					Neg.	20 yr.	Tabes.
		Clot	1392	15 S. 6 neo		0.6	35 min.	15.3376	5.1903	33.84	0.513	43	M. W.					Neg.	20 yr.	Tabes.
5	D. E.	S. F.	1452	15 S. 7 neo	19 S. E.	0.6	29 hr.	3.4882	0.0336	0.96	29.7	43	M. W.	3	Trace	++++ 2.0 c.c.	1111000000	Neg.	20 yr.	Tabes.
		Clot	1464	15 S. 7 neo		0.6	25 min.	23.0078	7.9082	34.37	2.27	43	M. W.					Neg.	20 yr.	Tabes.
	(Serum lost)																			
6	F. E.	S. F.	1114	7 neo	2 S. E.	0.6	32 hr.	3.1579	0.0371	1.17	2.60	40	M. W.	4	+	++++ 0.6 c.c.	2233210000	++++	8 yr.	C. S. L.; clinical symptoms.
		Serum	1115	7 neo		0.6	30 min.	3.6662	0.3534	9.63	0.56	40	M. W.					++++	8 yr.	C. S. L.; clinical symptoms.
		Clot	1123	7 neo		0.6	30 min.	17.3455	5.5655	32.08	0.167	40	M. W.					++++	8 yr.	C. S. L.; clinical symptoms.
6	F. E.	S. F.	1259	8 neo	3 S. E.	0.6	31½ hr.	3.0980	0.0320	1.01	0	40	M. W.	4	Trace	+++ 0.6 c.c.	2233210000	++++	8 yr.	C. S. L.; clinical symptoms.
		Serum	1260	8 neo		0.6	25 min.	3.4795	0.3475	10.0	34.3	40	M. W.					++++	8 yr.	C. S. L.; clinical symptoms.
		Clot	1258	8 neo		0.6	25 min.	18.4212	5.7310	31.11	0.0174	40	M. W.					++++	8 yr.	C. S. L.; clinical symptoms.
6	F. E.	S. F.	1405	9 neo	4 S. E.	0.6	31 hr.	3.8046	0.0397	1.04	25.1	40	M. W.	6	+	+++ 0.6 c.c.	1233210000	++++	8 yr.	C. S. L.; clinical symptoms.
		Serum	1406	9 neo		0.6	26 min.	3.2083	0.3278	10.20	2.03	40	M. W.					++++	8 yr.	C. S. L.; clinical symptoms.
		Clot	1413	9 neo		0.6	26 min.	18.5803	5.9003	31.75	0.339	40	M. W.					++++	8 yr.	C. S. L.; clinical symptoms.
6	F. E.	S. F.	1554	10 neo	5 S. E.	0.6	30 hr.	2.3832	0.0243	1.01	9.26	40	M. W.	6	+	++++ 0.6 c.c.	1233210000	++++	8 yr.	C. S. L.; clinical symptoms.
		Serum	1555	10 neo		0.6	25 min.	3.5893	0.3885	10.89	8.57	40	M. W.					++++	8 yr.	C. S. L.; clinical symptoms.
		Clot	1556	10 neo		0.6	25 min.	21.5761	6.9201	32.07	0.096	40	M. W.					++++	8 yr.	C. S. L.; clinical symptoms.
7	G. E.	S. F.	1009	13 S. 22 neo	33 S. E.	0.6	26¾ hr.	6.9837	0.0760	1.08	3.28	44	M. W.	3	Trace	++++ 0.4 c.c.	5555431000	+	21 yr.	Paresis; remission.
		Serum	1008	13 S. 22 neo		0.6	32 min.	3.4043	0.3111	9.13	0.32	44	M. W.					+	21 yr.	Paresis; remission.
7	G. E.	S. F.	1396	13 S. 23 neo	34 S. E.	0.6	28 hr.	3.7440	0.0415	1.108	24.0	44	M. W.	5	+	++++ 0.4 c.c.	5555431000	+	21 yr.	Paresis; remission.
		Serum	1397	13 S. 23 neo		0.6	30 min.	3.7105	0.3400	9.16	4.90	44	M. W.					+	21 yr.	Paresis; remission.
		Clot	1418	13 S. 23 neo		0.6	30 min.	27.5598	10.6783	38.74	0.075	44	M. W.					+	21 yr.	Paresis; remission.
8	H. T.	S. F.	1533	100 S. 3 neo	3 S. E.	0.6	30 hr.	3.6105	0.0336	0.93	1.49	42	M. W.	2	Trace	++++ 1.0 c.c.	1221000000	Neg.	23 yr.	C. S. L.; clinical symptoms.
		Serum	1534	100 S. 3 neo		0.6	23 min.	2.5990	0.2250	8.65	2.96	42	M. W.					Neg.	23 yr.	C. S. L.; clinical symptoms.
		Clot	1535	100 S. 3 neo		0.6	23 min.	22.7277	7.7114	30.39	0.129	42	M. W.					Neg.	23 yr.	C. S. L.; clinical symptoms.

TABLE I—Cont'd

CASE	PATIENT	SERIAL NO.	NO. PREVIOUS I. V. INJEC.	NO. PREVIOUS I. S. INJEC.	DOSE OF DRUG	TIME AFTER INJEC.	WT. OF SPECIMEN		PER CENT SOLIDS	AS. IN MG. PER 100 GMS. DRIED SPEC.	AGE	SEX AND COLOR	SPINAL FLUID FINDINGS				BLOOD WASS.	DURATION OF INFECTION	DIAGNOSIS AND REMARKS
							MOIST	DRY					CELLS	GLOB.	WASSERMANN	GOLD SOL.			
8	H. T. S. F.	1687	100 S. 4 neo	4 S. E.	0.6	29 hr.	3.0585	0.0270	0.88	3.70	42	M. W.	3	Trace	+++ 1.0 c.c.	1221000000	Neg.	23 yr.	C. S. L.; clinical symptoms.
	Serum	1688	100 S. 4 neo		0.6	15 min.	3.1265	0.2713	8.67	9.82	42	M. W.					Neg.	23 yr.	C. S. L.; clinical symptoms
	Clot	1690	100 S. 4 neo		0.6	15 min.	19.5118	6.3206	32.39	0	42	M. W.					Neg.	23 yr.	C. S. L.; clinical symptoms.
9	K. L. S. F.	1007	13 S. 4 neo	15 S. E.	0.6	28¾ hr.	5.7220	0.0600	1.04	1.66	40	M. W.	4	Trace	++++ 0.8 c.c.	1233210000	Neg.	Denied	C. S. L.; clinical manifestations.
	Serum	1006	13 S. 4 neo		0.6	30 min.	3.4986	0.3531	10.09	3.39	40	M. W.					Neg.	Denied	C. S. L.; clinical manifestations.
9	K. L. S. F.	1398	13 S. 5 neo	16 S. E.	0.6	28 hr.	4.6053	0.0493	1.07	23.6	40	M. W.	4	Trace	++ 0.8 c.c.	1233210000	Neg.	Denied	C. S. L.; clinical manifestations.
	Serum	1399	13 S. 5 neo		0.6	30 min.	2.8005	0.2724	9.72	11.0	40	M. W.					Neg.	Denied	C. S. L.; clinical manifestations.
	Clot	1417	13 S. 5 neo		0.6	30 min.	29.8755	9.8880	33.09	0.02	40	M. W.					Neg.	Denied	C. S. L.; clinical manifestations.
9	K. L. S. F.	1694	13 S. 6 neo	17 S. E.	0.6	29 hr.	3.6987	0.0359	0.97	0	40	M. W.	5	Trace	++++ 1.0 c.c.	1233210000	Neg.	Denied	C. S. L.; clinical manifestations.
	Serum	1695	13 S. 6 neo		0.6	21 min.	3.0025	0.2632	8.76	7.60	40	M. W.					Neg.	Denied	C. S. L.; clinical manifestations.
	Clot	1696	13 S. 6 neo		0.6	21 min.	29.2282	9.3032	31.82	0.214	40	M. W.					Neg.	Denied	C. S. L.; clinical manifestations.
10	K. E. S. F.	1449	1 SS. 10 neo	11 S. E.	0.6	29¾ hr.	4.3560	0.0478	1.09	83.6	40	M. W.	5	Trace	++++ 0.4 c.c.	5555431000	++++	20 yr.	Juvenile G. P. stationary.
	Clot	1466	1 SS. 10 neo		0.6	25 min.	18.8341	5.9370	31.52	1.59	40	M. W.					++++	20 yr.	Juvenile G. P. stationary.
11	M. Y. S. F.	1448	7 S. 23 neo	24 S. E.	0.6	31 hr.	3.7280	0.0396	1.06	Trace	48	M. W.	3	Trace	++++ 0.2 c.c.	5555431000	++++	Unknown	Paresis; clinical manifestations.
	Clot	1459	7 S. 23 neo		0.6	30 min.	13.9255	7.5005	33.52	0	48	M. W.					++++	Unknown	Paresis; clinical manifestations.
12	M. L. S. F.	1365	11 S. 4 neo	8 S. E.	0.6	29 hr.	3.8776	0.0321	0.83	12.4	36	M. W.	3	Trace	++++ 1.5 c.c.	1111000000	Neg.	?	C. S. L.; a symptomatic.
	Serum	1366	11 S. 4 neo		0.6	27 min.	3.3375	0.3053	9.14	0.49	36	M. W.					Neg.	?	C. S. L.; a symptomatic.
	Clot	1367	11 S. 4 neo		0.6	27 min.	20.8800	6.5550	31.39	6.86	36	M. W.					Neg.	?	C. S. L.; a symptomatic.
13	M. A. S. F.	1119	16 S. 17 neo	25 S. E.	0.6	25½ hr.	3.8020	0.0420	1.10	3.50	39	M. W.	4	+	++++ 0.4 c.c.	5555321000	++++	15 yr.	Optic atrophy; paresis; clinical manifestations.
	Serum	1141	16 S. 17 neo		0.6	30 min.	4.3860	0.4050	9.23	1.72	39	M. W.					++++	15 yr.	Optic atrophy; paresis; clinical manifestations.
	Clot	1108	16 S. 17 neo		0.6	30 min.	24.7074	10.4698	42.37	0.057	39	M. W.					++++	15 yr.	Optic atrophy; paresis; clinical manifestations.
13	M. A. S. F.	1218	16 S. 18 neo	26 S. E.	0.6	24¼ hr.	4.4540	0.0478	1.08	3.10	39	M. W.	5	+	++++ 0.4 c.c.	5555321000	++++	15 yr.	Optic atrophy; paresis; clinical manifestations.
	Serum	1219	16 S. 18 neo		0.6	25 min.	4.0951	0.3684	9.00	2.17	39	M. W.					++++	15 yr.	Optic atrophy; paresis; clinical manifestations.
	Clot	1217	16 S. 18 neo		0.6	25 min.	25.3705	9.7976	38.60	0.005	39	M. W.					++++	15 yr.	Optic atrophy; paresis; clinical manifestations.
13	M. A. S. F.	1451	16 S. 19 neo	27 S. E.	0.6	29 hr.	3.3176	0.0349	1.05	2.87	39	M. W.	6	+	++++ 0.4 c.c.	5555321000	++++	15 yr.	Optic atrophy; paresis; clinical manifestations.
	Serum	1457	16 S. 19 neo		0.6	25 min.	18.1118	5.8253	32.16	1.03	39	M. W.					++++	15 yr.	Optic atrophy; paresis; clinical manifestations.

TABLE I—Cont'd

14	R. N.	S. F.	1182	10 S. 8 neo	6 S. E.	0.6	29 hr.	4.8637	0.0458	0.94	1.09	39	M. W.	5	Trace	++++ 0.4 c.c.	2233210000	++++	15 yr.	Optic atrophy; Tabes dorsalis; active.
		Serum	1183	10 S. 8 neo		0.6	40 min.	3.3922	0.2862	8.44	1.04	39	M. W.					++++	15 yr.	Optic atrophy; Tabes dorsalis; active.
		Clot	1190	10 S. 8 neo		0.6	40 min.	13.1896	5.5424	42.02	0.206	39	M. W.					++++	15 yr.	Optic atrophy; Tabes dorsalis; active.
15	R. H.	S. F.	1404	6 S. 15 neo	4 S. E.	0.6	31¼ hr.	2.9265	0.0342	1.16	35.08	32	M. W.	4	Trace	++++ 0.2 c.c.	5555431000	++++	16 yr.	Tabo-paresis; clinical manifestations.
		Clot	1414	6 S. 15 neo		0.6	20 min.	23.5825	6.0250	25.54	0.331	32	M. W.					++++	16 yr.	Tabo-paresis; clinical manifestations.
15	R. H.	S. F.	1560	6 S. 16 neo	5 S. E.	0.6	31 hr.	3.5634	0.0380	1.06	2.63	32	M. W.	4	+	++++ 0.2 c.c.	5555431000	++++	16 yr.	Tabo-paresis; clinical manifestations.
		Serum	1561	6 S. 16 neo		0.6	30 min.	1.7672	0.1816	10.27	11.0	32	M. W.					++++	16 yr	Tabo-paresis; clinical manifestations.
		Clot	1562	6 S. 16 neo		0.6	30 min.	27.0701	9.9661	36.81	0.411	32	M. W.					++++	16 yr.	Tabo-paresis; clinical manifestations.
15	R. H.	S. F.	1710	6 S. 17 neo	6 S. E.	0.6	28 hr.	3.9558	0.0420	1.06	4.76	32	M. W.	5	+	++++ 0.2 c.c.	5555431000	++++	16 yr.	Tabo-paresis; clinical manifestations.
		Serum	1711	6 S. 17 neo		0.6	16 min.	2.6337	0.2294	8.71	0.435	32	M. W.					++++	16 yr.	Tabo-paresis; clinical manifestations.
		Clot	1712	6 S. 17 neo		0.6	16 min.	11.5247			0.087 (moist)	32	M. W.					++++	16 yr.	Tabo-paresis; clinical manifestations.
16	S. R.	S. F.	1178	30 S. 10 neo	10 S. E.	0.6	29 hr.	4.4914	0.0484	1.08	5.16	44	M. W.	3	Trace	+++ 0.6 c.c.	1122100000	+ −	23 yr.	Tabes dorsalis; clinically positive.
		Serum	1179	30 S. 10 neo		0.6	27 min.	3.3155	0.2884	8.70	1.04	44	M. W.					+ −	23 yr.	Tabes dorsalis; clinically positive.
		Clot	1189	30 S. 10 neo		0.6	27 min.	16.8600	7.3225	43.43	0.116	44	M. W.					+ −	23 yr.	Tabes dorsalis; clinically positive.
16	S. R.	S. F.	1566	30 S. 11 neo	11 S. E.	0.6	30 hr. 25 min.	2.9053	0.0301	1.03	Trace	44	M. W.	2	Trace	++++ 0.6 c.c.	1122100000	+ −	23 yr.	Tabes dorsalis; clinically positive.
		Serum	1567	30 S. 11 neo		0.6	35 min.	4.0951	0.4083	9.97	1.46	44	M. W.					+ −	23 yr.	Tabes dorsalis; clinically positive.
		Clot	1568	30 S. 11 neo		0.6	35 min.	32.9218	8.8549	26.89	0.677	44	M. W.					+ −	23 yr.	Tabes dorsalis; clinically positive.
17	S. N.	S. F.	1089	16 S. 18 neo	28 S. E.	0.45	31 hr.	3.8100	0.0407	1.06	Trace	62	M. W.	6	+	+++ 0.8 c.c.	1123210000	++++	30 yr.	Meningo-vasculitis; fluid had been strongly positive.
		Serum	1090	16 S. 18 neo		0.45	30 min.	4.1550	0.3867	9.30	Trace	62	M. W.					++++	30 yr.	Meningo-vasculitis; fluid had been strongly positive.
		Clot	1124	16 S. 18 neo		0.45	30 min.	17.8073	5.6873	31.93	0.18	62	M. W.					++++	30 yr.	Meningo-vasculitis; fluid had been strongly positive.
17	S. N.	S. F.	1557	16 S. 19 neo	29 S. E.	0.5	30¾ hr.	3.0975	0.0333	1.07	Trace	62	M. W.	2	Trace	++++ 0.8 c.c.	1123210000	++++	30 yr.	Meningo-vasculitis; fluid had been strongly positive.
		Serum	1558	16 S. 19 neo		0.5	30 min.	4.0869	0.3857	9.45	5.18	62	M. W.					++++	30 yr.	Meningo-vasculitis; fluid had been strongly positive.
		Clot	1559	16 S. 19 neo		0.5	30 min.	21.0523	6.7269	31.95	0.297	62	M. W.					++++	30 yr.	Meningo-vasculitis; fluid had been strongly positive.
18	S. A.	S. F.	1165	8 S. 6 neo	3 S. E.	0.6	29½ hr.	6.4816	0.0836	1.29	0.615	46	M. W.	5	+	++++ 0.8 c.c.	1123210000	Neg.	25 yr.	C. S. L.; asymptomatic.
		Serum	1035	8 S. 6 neo		0.6	31 min.	4.0390	0.3823	9.46	8.60	46	M. W.					Neg.	25 yr.	C. S. L.; asymptomatic.
		Clot	1036	8 S. 6 neo		0.6	31 min.	26.2195	9.6740	36.89	0.031	46	M. W.					Neg.	25 yr.	C. S. L.; asymptomatic.
18	S. A.	S. F.	1186	8 S. 7 neo	4 S. E.	0.6	31½ hr.	3.7300	0.0398	1.07	81.9	46	M. W.	4	Trace	++++ 1.0 c.c.	1123210000	Neg.	25 yr.	C. S. L.; asymptomatic.
		Serum	1185	8 S. 7 neo		0.6	37 min.	3.4884	0.3094	8.87	7.70	46	M. W.					Neg.	25 yr.	C. S. L.; asymptomatic.
		Clot	1184	8 S. 7 neo		0.6	37 min.	24.8606	11.3477	45.65	0.053	46	M. W.					Neg.	25 yr.	C. S. L.; asymptomatic.

TABLE I—Cont'd

CASE	PATIENT		SERIAL NO.	NO. PREVIOUS I. V. INJEC.	NO. PREVIOUS I. S. INJEC.	DOSE OF DRUG	TIME AFTER INJEC.	WT. OF SPECIMEN		PER CENT SOLIDS	AS. IN MG. PER 100 GMS. DRIED SPEC.	AGE	SEX AND COLOR	SPINAL FLUID FINDINGS				BLOOD WASS.	DURATION OF INFECTION	DIAGNOSIS AND REMARKS
								MOIST	DRY					CELLS	GLOB.	WASSERMANN	GOLD SOL			
18	S. A.	S. F.	1450	8 S. 8 neo	5 S. E.	0.6	29¼ hr.	3.5750	0.0367	1.02	8.17	46	M. W.	2	Trace	++++ 1.0 c.c.	1123210000	Neg.	25 yr.	C. S. L.; asymptomatic.
		Clot	1458	8 S. 8 neo		0.6	26 min.	15.6308	7.5760	32.14	0.422	46	M. W.					Neg.	25 yr.	C. S. L.; asymptomatic.
18	S. A.	S. F.	1691	8 S. 9 neo	6 S. E.	0.6	29 hr.	2.2674	0.0195	0.86	0	46	M. W.	3	Trace	++++ 1.0 c.c.	1123210000	Neg.	25 yr.	C. S. L.; asymptomatic.
		Serum	1692	8 S. 9 neo		0.6	16 min.	2.5450	0.2268	8.91	6.61	46	M. W.					Neg.	25 yr.	C. S. L.; asymptomatic.
		Clot	1693	8 S. 9 neo		0.6	16 min.	24.9690	7.7662	31.10	0.039	46	M. W.					Neg.	25 yr.	C. S. L.; asymptomatic.
19	S. E.	S. F.	1113	9 neo	3 S. E.	0.6	26 hr.	5.2688	0.0605	1.14	Trace	38	M. W.	3	+	++++ 0.2 c.c.	5555431000	++++	Denied	Paresis; clinical manifestations.
		Serum	1117	9 neo		0.6	30 min.	3.0902	0.2947	9.53	4.50	38	M. W.					++++	Denied	Paresis; clinical manifestations.
		Clot	1107	9 neo		0.6	30 min.	26.5934	11.1080	41.76	0.054	38	M. W.					++++	Denied	Paresis; clinical manifestations.
20	S. S.	S. F.	1445	10 S. 14 neo	7 S. E.	0.6	50 hr.	2.9825	0.0325	1.08	1.53	44	M. W.	6	Trace	++++ 1.0 c.c.	1233210000	+	22 yr.	C. S. L.; clinical manifestations.
		Clot	1462	10 S. 14 neo		0.6	30 min.	30.5709	12.9684	42.42	0.616	44	M. W.					+	22 yr.	C. S. L.; clinical manifestations.
21	S. G.	S. F.	1447	1 neo	1 S. E	0.45	26 hr.	3.1130	0.0341	1.09	2.93	36	F. W.	1	Trace	+ 2.0 c.c.	1122100000	Neg.	12 yr.	Tabes; clinical symptoms.
		Clot	1460	1 neo		0.45	25 min.	23.0550	7.3260	31.77	0.041	36	F. W.					Neg.	12 yr.	Tabes; clinical symptoms.
22	V. N.	S. F.	1085	5 S. 8 neo	4 S. E.	0.6	32 hr.	5.5147	0.0596	1.08	0	51	M. W.	7	+	++++ 0.2 c.c.	5554310000	++++	15 yr.	Neurosyphilis; paretic type.
		Serum	1086	5 S. 8 neo		0.6	30 min.	3.4291	0.2931	8.54	13.0	51	M. W.					++++	15 yr.	Neurosyphilis; paretic type.
22	V. N.	S. F.	1387	5 S. 9 neo	5 S. E.	0.6	7½ hr.	4.2423	0.0433	1.02	69.0	51	M. W.	5	+	++++ 0.2 c.c.	5554310000	++++	15 yr.	Neurosyphilis; paretic type.
		Serum	1388	5 S. 9 neo		0.6	25 min.	3.4040	0.2905	8.53	13.7	51	M. W.					++++	15 yr.	Neurosyphilis; paretic type.
		Clot	1297	5 S. 9 neo		0.6	25 min.	19.1740	7.0773	36.91	0.014	51	M. W.					++++	15 yr.	Neurosyphilis; paretic type.
22	V. N.	S. F.	1409	5 S. 10 neo	6 S. E.	0.6	30 hr.	4.9105	0.0540	1.09	74.0	51	M. W.	4	++	++++ 0.2 c.c.	5554310000	++++	15 yr.	Neurosyphilis; paretic type.
		Serum	1410	5 S. 10 neo		0.6	30 min.	2.8108	0.2529	8.809	5.93	51	M. W.					++++	15 yr.	Neurosyphilis; paretic type.
		Clot	1411	5 S. 10 neo		0.6	30 min.	22.7096	8.2370	36.27	0.121	51	M. W.					++++	15 yr.	Neurosyphilis; paretic type.
23	W. L.	S. F.	1453	23 S. 20 neo	32 S. E.	0.6	27 hr.	4.3030	0.0435	1.01	36.7	36	M. W.	2	Trace	Neg. 2.0 c.c.	1112100000	Neg.	Unknown	C. S. L.; had been strongly positive.
		Clot	1465	23 S. 20 neo		0.6	28 min.	30.9317	10.7090	34.62	0.56	36	M. W.					Neg.	Unknown	C. S. L.; had been strongly positive.
24	W. J.	S. F.	1016	22 S. 5 neo	22 S. E.	0.6	28¾ hr.	5.0042	0.0511	1.02	6.84	31	M. W.	5	Trace	+++ 1.5 c.c.	0000000000	+ —	10 yr.	C. S. L.; asymptomatic.
		Serum	1015	22 S. 5 neo		0.6	30 min.	4.2915	0.3900	9.08	0.256	31	M. W.					+ —	10 yr.	C. S. L.; asymptomatic.
25	W. G.	S. F.	1180	14 neo	11 S. E.	0.45	27 hr.	4.3523	0.0437	1.00	1.14	14	F. W.	3	Trace	++++ 0.1 c.c.	5555432000	++++	14 yr.	Meningo-vasculitis? Juvenile paresis? Clinical manifestations.
		Serum	1181	14 neo		0.45	20 min.	4.1860	0.3723	8.95	1.60	14	F. W.					++++	14 yr.	Meningo-vasculitis? Juvenile paresis? Clinical manifestations.
		Clot	1187	14 neo		0.45	20 min.	14.9645	5.8773	39.28	0.119	14	F. W.					++++	14 yr.	Meningo-vasculitis? Juvenile paresis? Clinical manifestations.

TABLE I—Cont'd

25	W. G. S. F.	1371	15 neo	12 S. E.	0.45	26 hr.	1.8819	0.0305	1.62	19.6	14	F. W.	4	Trace	+++ 0.1 c.c.	5555432000	++++	14 yr.	Meningo-vasculitis? Juvenile paresis? Clinical manifestations.
	Serum	1372	15 neo		0.45	20 min.	4.2893	0.4015	9.33	3.73	14	F. W.					++++	14 yr.	Meningo-vasculitis? Juvenile paresis? Clinical manifestations.
	Clot	1373	15 neo		0.45	20 min.	18.5648	5.7595	31.02	0.017	14	F. W.					++++	14 yr.	Meningo-vasculitis? Juvenile paresis? Clinical manifestations.
26	W. N. S. F.	1256	8 neo	6 S. E.	0.6	25 hr.	2.5209	0.0270	1.07	0	39	M. W.	2	Trace	± 2.0 c.c.	0000000000	Neg.	19 yr.	Tabes dorsalis. Now asymptomatic clinically.
	Serum	1257	8 neo		0.6	25 min.	3.7380	0.3905	10.20	3.15	39	M. W.					Neg.	19 yr.	Tabes dorsalis. Now asymptomatic clinically.
	Clot	1255	8 neo		0.6	25 min.	22.8690	7.8740	34.43	0.076	39	M. W.					Neg.	19 yr.	Tabes dorsalis. Now asymptomatic clinically.
26	W. N. S. F.	1572	9 neo	7 S. E.	0.6	28 hr.	3.0650	0.0340	1.109	51.4	39	M. W.	4	Trace	± 2.0 c.c.	0000000000	Neg.	19 yr.	Tabes dorsalis. Now asymptomatic clinically.
	Serum	1573	9 neo		0.6	20 min.	3.0103	0.2923	9.71	20.5	39	M. W.					Neg.	19 yr.	Tabes dorsalis. Now asymptomatic clinically.
	Clot	1574	9 neo		0.6	20 min.	17.3168	5.9204	34.18	0.405	39	M. W.					Neg.	19 yr.	Tabes dorsalis. Now asymptomatic clinically.
27	Y. G. S. F.	1087	8 neo	4 S. E.	0.6	29 hr. 40 min.	4.9873	0.0547	1.09	0	40	M. W.	4	Trace	++++ 0.6 c.c.	1122100000	Neg.	20 yr.	Tabes dorsalis, clinically positive.
	Serum	1088	8 neo		0.6	30 min.	3.2826	0.3066	9.34	Trace	40	M. W.					Neg.	20 yr.	Tabes dorsalis, clinically positive.
27	Y. G. S. F.	1253	9 neo	5 S. E.	0.6	31 hr.	4.8450	0.0515	1.06	11.6	40	M. W.	3	Trace	++++ 0.6 c.c.	1122100000	Neg.	20 yr.	Tabes dorsalis, clinically positive.
	Serum	1254	9 neo		0.6	25 min.	3.0020	0.3002	10.0	7.30	40	M. W.					Neg.	20 yr.	Tabes dorsalis, clinically positive.
	Clot	1252	9 neo		0.6	25 min.	28.7413	10.3933	36.16	0.019	40	M. W.					Neg.	20 yr.	Tabes dorsalis, clinically positive.

TABLE II

ARSENIC CONTENT OF SPINAL FLUID OF PATIENTS TREATED BY THE SWIFT-ELLIS METHOD WITH NEOSALVARSAN, GROUPED ACCORDING TO CLINICAL DIAGNOSIS AND QUANTITY FOUND

		No Arsenic		
Tabes	Case 1	0.6 gm.	30 hours	
	“ 2	0.6 “	25 “	
	“ 3	0.6 “	30 “	
Paresis	“ 4	0.6 “	32 “	
Cerebro-spinal Syphilis	“ 5	0.6 “	29 “	
	“ 6	0.6 “	31½ “	
	“ 7	0.75 “	29 “	
		Indeterminate Amounts of Arsenic		
Tabes	Case 8	0.6 gm.	30 hours	
	“ 1	0.6 “	32 “	
Paresis	“ 9	0.6 “	26 “	
	“ 10	0.6 “	31 “	
Cerebro-spinal Syphilis	“ 11	0.45 “	31 “	
	“ 11	0.5 “	31 “	
		From 0.6 to 5 Milligrams of Arsenic per 100 gm. dried specimen.		
Tabes	Case 12	0.6 gm.	29 hours	1.09 mg.
	“ 13	0.45 “	26 “	2.93 “
Paresis	“ 14	0.6 “	27 “	3.28 “
	“ 15	0.6 “	29 “	2.87 “
		0.6 “	24½ “	3.10 “
		0.6 “	25½ “	3.50 “
	“ 16	0.6 “	31 “	2.63 “
		0.6 “	28 “	4.76 “
	“ 17	0.6 “	26 “	2.33 “
	“ 18	0.45 “	27 “	1.14 “
Cerebro-spinal Syphilis	“ 19	0.6 “	30 “	1.49 “
		0.6 “	29 “	3.70 “
	“ 7	0.6 “	29 “	1.66 “
	“ 20	0.6 “	50 “	1.53 “
	“ 21	0.6 “	30 “	2.07 “
	“ 22	0.6 “	50 “	1.93 “
	“ 6	0.6 “	32 “	2.60 “
	“ 5	0.6 “	29½ “	0.615 “

TABLE II—CONT'D

From 5 to 20 Milligrams of Arsenic per 100 gm. dried specimen.

Tabes	Case	3	0.6	gm.	31	hours	11.6	mg.
	"	8	0.6	"	29	"	5.16	"
Paresis	"	18	0.45	"	26	"	19.6	"
	"	23	0.6	"	29½	"	16.0	"
	"	17	0.6	"	30	"	5.83	"
Cerebro-spinal Syphilis	"	24	0.6	"	29	"	12.4	"
	"	25	0.6	"	28¾	"	6.84	"
	"	6	0.6	"	30	"	9.26	"
	"	5	0.6	"	29	"	8.17	"
	"	22	0.6	"	29	"	5.70	"
	"	22	0.6	"	30	"	12.0	"
	"	22	0.6	"	52	"	9.30	"

From 20 to 50 Milligrams of Arsenic per 100 gm. dried specimen.

Tabes	Case	1	0.6	gm.	29	hours	29.7	mg.
Paresis	"	23	0.6	"	29	"	21.	"
	"	16	0.6	"	31¼	"	35.08	"
	"	14	0.6	"	28	"	24.	"
Cerebro-spinal Syphilis	"	6	0.6	"	31	"	25.01	"
	"	7	0.6	"	28	"	23.6	"
	"	26	0.6	"	27	"	36.7	"

From 50 to 83.6 Milligrams of Arsenic per 100 gm. dried specimen.

Tabes	Case	2	0.6	gm.	28	hours	51.4	mg.
Paresis	"	4	0.6	"	7½	"	69.	"
	"	4	0.6	"	30	"	74.	"
	"	23	0.6	"	29¾	"	65.5	"
	"	27	0.5	"	30	"	83.6	"
Cerebro-spinal Syphilis	"	5	0.6	"	31½	"	81.9	"

SUMMARY

1. The serum, clot and cerebrospinal fluid of 27 patients treated with neo-salvarsan intravenously and auto-serum intraspinally were analyzed for arsenic content.

2. Complete serological findings and arsenic determinations are recorded in the histories of the cases and in Table I. A classification based on the type of neurosyphilis and the amount of arsenic demonstrated in the cerebro-spinal fluid will be found in Table II.

3. As mentioned in this article, as well as in a previous communication dealing with the values for arsenic, it must be remembered at all times that whenever an arsenic value is stated, the authors have in mind the arsenic content of the specimen in milligrams of metallic arsenic per 100 grams of dried specimen.

4. In these investigations it was found that 26 per cent of the patients and 12.5 per cent of the cerebro-spinal fluids showed no arsenic at the time of at least one examination. Each patient showing these negative findings at some other time yielded fluid containing arsenic.

Twenty-two per cent of the patients or 10.5 per cent of the cerebrospinal fluids showed a trace of arsenic at some time during the treatment.

Thirty-four per cent of the spinal fluids yielded 0.6 to 5 mg.; 21 per cent of fluids 5 to 20 mg.; 12.5 per cent showed 20 to 50 mg.; and 10.5 per cent yielded 50 to 83.6 mg. of metallic arsenic per 100 grams of dried specimen.

5. These analyses indicate that arsenic passes with comparative ease into the spinal fluid in probably every individual at some period during the course of treatment. In one patient on whom four determinations were made at intervals of 30 hours after each intravenous treatment no arsenic was found at one examination, while another yielded 81.9 mg. per 100 grams of dried specimen, or 0.819 mg. per 100 c.c. of spinal fluid.

6. An attempt will be made in further studies to determine the factors related to the quantitative variations in different individuals.

7. Referring to the Combination Chart (Table I), it will be seen that the average percentage of solids of the spinal fluid was found to be 1.07; the highest percentage was 1.62 and the lowest 0.83. Generally speaking 0.9 is regarded as the normal percentage of solids for the spinal fluid. The significance of these values has not been correlated at the present time. Eight patients with decreasing total solids showed a marked improvement; 8 in whom the percentage was high and remained so were stationary from a clinical standpoint, while four showing an increasing percentage were not making favorable clinical progress.

8. The Combination Chart (Table I) further shows the partition of the arsenic in the serum and clot, indicating that the method employed for separating the serum to be used for intraspinal therapy

is an efficient one when carried out according to our procedure. The partition co-efficient of the arsenic in the serum is a variable of the same magnitude, as pointed out in the previous article No. IV, dependent upon certain biological characteristics of the individual. It is also manifest that these variations of the partition co-efficient of arsenic in the serum is a factor which probably also influences the amount of arsenic found in the spinal fluid at later examinations.

9. Discussion of the clinical results and theoretical considerations connected with them will be found at the close of this series.

QUANTITATIVE STUDIES IN SYPHILIS FROM A CLINICAL AND BIOLOGICAL POINT OF VIEW

VI. Arsenic Content of the Spinal Fluid after Salvarsan in the Swift-Ellis Method of Treatment

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The analytical studies on the cerebro-spinal fluid which form the subject of this article were conducted on lines similar to those reported in No. V of this series. Salvarsan, however, was used instead of neosalvarsan.

The investigations were made on 62 patients suffering from various types of neurosyphilis, many of them in an advanced stage of the disease. A total of 257 spinal fluids was examined at the different intervals stated in the tables.

These patients received an intravenous injection of salvarsan prepared according to the technic described in article IV and were treated intraspinally with autogenous sera where the intervals were 24 hours or longer. Where a spinal fluid was removed for analytical purposes one half to four hours after an intravenous injection the patient was treated with salvarsanized serum obtained the day before from another case as there was not time to prepare an autoserum at these short intervals.

The following histories of cases on whom repeated arsenic determinations were made are appended to show the variations quantitatively which may occur in the same patient. Reference should be made to articles I and V for a discussion of the method of calculating the amount of arsenic found in these specimens.

Meningo-encephalitis: J. B., Male; colored; age 28; chancre November, 1919. Treatment begun six weeks later with appearance of rash. After 8 salvarsan and 12 mercury injections discontinued treatment for one month, then developed iritis, deafness and a week later right sided facial palsy with left sided palsy two days later. Was dizzy, unsteady and staggered. He received syphilitic treatment from his physician and prominent symptoms yielded rapidly.

Physical examination: When seen two months later showed residua of facial paralysis; all deep reflexes were very active and greater on the left side.

Serology:	Blood	3/24/20	++++
		7/28/20	Negative
	Spinal fluid	3/24/20	Cells 210 Glob. ++++ Wass. ++++ to 0.4 c.c. Gold Sol: Paretic curve
		5/27/21	Cells 3 Glob. trace Wass. ++++ with 1.0 c.c. Gold Sol: Luetic curve

Results: He was placed on further intravenous treatment combined with drainage. His fluid became almost negative, but after the 9th drainage became stronger than it had been in the beginning, the cells having increased to 280. Intraspinal injections were then given and the fluid gradually returned to normal.

Treatment and Arsenic Determinations:

PREVIOUS NO. I. V. INJECTIONS	PREVIOUS NO. I. S. INJECTIONS	DOSE	INTERVAL AFTER I. V.	AS PER 100 GM. DRIED SPEC.
17	9 Dr. 3 S.E	0.4 gm.	48 hours	6.9 mg.
18	9 Dr. 4 S.E	0.4 "	24 "	4.7 "
19	9 Dr. 5 S.E	0.4 "	48 "	0. "
21	9 Dr. 6 S.E	0.4 "	48 "	1.5 "
23	9 Dr. 8 S.E	0.4 "	48 "	trace
24	9 Dr. 9 S.E	0.4 "	48 "	0.64 mg.

Remarks: Prior to the third intraspinal injection, which showed the highest value, four weekly intravenous injections had been received. The intervals between the other injections were two weeks, excepting before the sixth, when it was six weeks.

CEREBROSPINAL SYPHILIS: J. M., Male, age 34, chancre in 1911, secondaries denied; had one salvarsan and 15 injections of mercury. In 1919 had hemiplegia of right side which disappeared under treatment in about two months.

Took treatment spasmodically from this time until Sept. 1921 when he first came under observation.

Physical examination: Pupils unequal, right fixed to light, left very sluggish. All deep reflexes very active especially on the right side. Gait normal, other findings negative.

Serology:	Blood	9/30/21	++++
		6/ 9/22	++
	Spinal Fluid	9/30/21	Cells 3
			Glob. +
			Wass. 3+ to 0.4 c.c.
			Gold Sol: Luetic curve
		6 /9/22	Cells 2
			Glob. trace
			Wass. 3+ to 1.0 c.c.
			Gold Sol: Luetic curve

Results: Patient developed no further symptoms while under observation and his spinal fluid has gradually become negative.

Treatment and arsenic determinations:

PREVIOUS NO. I. V. INJECTIONS	PREVIOUS NO. I. S. INJECTIONS	DOSE	INTERVAL AFTER I. V.	AS PER 100 GM. DRIED SPEC.
1	1	0.4 gm.	48 hours	None
3	3	0.3 "	24 "	3.05 mg.
4	4	0.3 "	48 "	7.4 "
5	5	0.3 "	½ "	4.1 "
7	7	0.3 "	2 "	1.32 "
8	8	0.3 "	48 "	None
9	9	0.3 "	24 "	2.9 "
10	10	0.3 "	24 "	23.0 "
11	11	0.4 "	2 "	2.48 "
12	12	0.3 "	48 "	3.83 "

Remarks: The first ten combined treatments were taken at the rate of two a month; the largest amount 23.0 mg. appeared at the end of the series. This was followed by a rest of three and one-half months, when the 11th and 12th treatments were taken two weeks apart.

TABES: S. M., male, age 42, chancre 1903 with secondaries. Came to the clinic with a gumma of the thigh; no symptoms referable to the nervous system.

Physical examination: Pupils small; regular, equal, fixed to light. Hearing slightly impaired; upper deep reflexes diminished on both sides. Patellar and ankle jerks absent. Slight Rhomberg. Tactile sensation diminished.

Serology:	Blood	3/ 2/20	++++
		10/31/22	++++

Spinal Fluid 3/ 2/20 Cells 45
Glob. ++++
Wass. ++++ to 0.2 c.c.
Gold Sol: luetic curve
10/31/22 Cells 1
Glob. Negative
Wass. ++++ with 0.6 c.c.
Gold Sol: luetic curve

Results: Patient has continued well subjectively; the serological findings are gradually becoming weaker under treatment. The objective findings have remained the same.

Treatment and Arsenic determinations:

PREVIOUS NO. I. V. INJECTIONS	PREVIOUS NO. I. S. INJECTIONS	DOSE	INTERVAL AFTER I. V.	AS PER 100 GM. DRIED SPEC.
25	8	0.4 gm.	2 hours	9.09 mg.
26	9	0.4 "	2 "	13.1 "
27	10	0.4 "	48 "	0.41 "
28	11	0.4 "	2 "	5.0 "
29	12	0.4 "	3 "	trace
30	13	0.4 "	2 "	trace
31	14	0.4 "	2 "	1.7 "

Remarks: The low values followed intervals of one and one-half to two and one-half months; the large ones two and three week intervals.

MENINGOVASCULITIS: E. A., male, age 29, chancre nine years ago, no secondaries. Came to the Clinic complaining of dizziness, headache and sore throat.

Physical examination: Pupils equal, regular, react very sluggishly to light. All deep reflexes very active and slightly unequal on the two sides. Other physical findings negative.

Serology: Blood 9/28/20 ++++
9/13/22 negative
Spinal Fluid 9/28/20 Cells 60
Glob. ++++
Wass. ++++ to 0.1 c.c.
Gold Sol: Paretic curve
6/13/22 Cells 5
Glob. ++
Wass. +++ with 0.2 c.c.
Gold Sol: Luetic curve

Results: Patient no longer has headaches or dizziness and feels entirely well in every way. The Wassermann in his spinal fluid is still positive although much weaker than recorded above and the colloidal gold curve has changed from the paretic to the luetic type.

Treatment and arsenic determinations:

PREVIOUS NO. I. V. INJECTIONS	PREVIOUS NO. I. S. INJECTIONS	DOSE	INTERVAL AFTER I. V.	AS PER 100 GM. DRIED SPEC.
36	6	0.4 gm.	48 hours	0.15 mg.
38	7	0.4 "	48 "	8.8 "
39	8	0.4 "	48 "	14.7 "
40	9	0.4 "	48 "	1.43 "
41	10	0.4 "	48 "	0. "
42	11	0.4 "	24 "	2.2 "
44	12	0.4 "	3 "	trace
51	14	0.4 "	48 "	31.3 "

Remarks: These treatments were taken very irregularly with intervals of three weeks to seven weeks to five months. The 14.7 mg. appeared after a seven week interval and the 31.3 mg. after one of five months.

TABES: C. G., male, age 35, chancre in 1907 followed by secondaries. In 1913 had a gumma of the palate destroying the uvula.

Physical examination: Pupils round, equal, react slowly to light; deep reflexes of upper extremities active and equal; patellar and ankle jerks absent; superficial reflexes present and equal; slight Rhomberg; no sensory disturbances; no ataxia.

Serology:	Blood	7/20/18	++++
		2/23/19	negative
	Spinal Fluid	7/20/18	Cells negative
			Glob. negative
			Wass. ++++ with 0.4 c.c.
			Gold Sol: Luetic curve
		2/23/19	Cells negative
			Glob. negative
			Wass. ++++ with 1.5 c.c.
			Gold Sol: Luetic curve

Results: He has remained well subjectively; physical findings continue as above. Spinal fluid gradually reduced to negative.

Treatment and arsenic determinations:

PREVIOUS NO. I. V. INJECTIONS	PREVIOUS NO. I. S. INJECTIONS	DOSE	INTERVAL AFTER I. V.	AS PER 100 GM. DRIED SPEC.
54	34	0.4 gm.	24 hours	17.2 mg.
55	35	0.4 "	24 "	.79 "
56	36	0.4 "	24 "	2.9 "
58	37	0.4 "	24 "	3.40 "
63	38	0.4 "	24 "	0. "
64	39	0.4 "	24 "	1.83 "
65	40	0.4 "	24 "	2.04 "
66	41	0.4 "	24 "	12.0 "

Remarks: Preceding the highest value, 17.2 mg., patient had had two intravenous injections of 0.4 gm. salvarsan five days apart. The intervals between the other treatments were two, three and four weeks; a negative fluid and one containing 12 mg. were both obtained after two week intervals.

TABES: E. K., female, age 32, no history of syphilis. In 1919 a routine examination disclosed a positive Wassermann. Was given 30 salvarsan and 30 mercurial injections. Was first seen in August, 1920 when she complained of double vision and pains in the lumbar region.

Physical examination: Pupils equal; react to light and accommodation; slight internal strabismus left eye; deep reflexes upper extremities weak; patellar and Achilles absent. Superficial reflexes sluggish. Sensation, gait and station normal.

Serology:	Blood	8/12/20	Negative
		6/ 9/21	Negative
	Spinal Fluid	9/14/20	Cells 10 Glob. + Wass. ++++ to 0.2 c.c. Gold Sol: Luetic curve
		6/ 9/21	Cells 4 Glob. + Wass. ++++ to 0.6 c.c. Gold Sol: Luetic curve

Results: Strabismus and pains disappeared; no further symptoms have developed since.

Treatment and arsenic determinations:

PREVIOUS NO. I. V. INJECTIONS	PREVIOUS NO. I. S. INJECTIONS	DOSE	INTERVAL AFTER I. V.	AS PER 100 GM. DRIED SPEC.
6	1	0.3 gm.	24 hours	2.64 mg.
7	2	0.3 "	24 "	8.47 "
9	4	0.3 "	24 "	6.90 "
10	5	0.3 "	48 "	3.50 "
11	6	0.3 "	24 "	4.30 "
12	7	0.3 "	24 "	trace

Remarks: The intervals between the above treatments were two, three and four weeks. That before removal of the fluid showing a trace was four weeks.

CEREBROSPINAL SYPHILIS: L. V., male, age 35, chancre and secondary rash in 1907 for which he took mercury and iodide for 5 years. Was gassed in France in 1916. Failing vision six months later; in the latter part of January, 1919, diplopia.

Physical examination: Pupils unequal; irregular; fixed to light. Partial ptosis of left eyelid; and external strabismus. Upper reflexes present; lower reflexes more active on left side, otherwise negative.

Serology:	Blood	2/28/19	++++
		5/15/21	+
	Spinal Fluid	3/21/19	Cells 56 Glob. ++++ Wass. ++++ to 0.2 c.c. Gold Sol: Luetic curve
		5/15/21	Cells 2 Glob. + Wass. ++++ to 0.4 c.c. Gold Sol: Luetic curve

Results: Paralysis of eye cleared entirely. Pupils remained the same; patient feels well but Wassermann in fluid remains strongly positive.

Treatment and arsenic determinations:

PREVIOUS NO. I. V. INJECTIONS	PREVIOUS NO. I. S. INJECTIONS	DOSE	INTERVAL AFTER I. V.	AS PER 100 GM. DRIED SPEC.
36	29	0.4 gm.	24 hours	8.0 mg.
37	30	0.4 "	24 "	20. "
38	31	0.4 "	24 "	7.90 "
39	32	0.4 "	24 "	23.90 "
41	33	0.4 "	48 "	0.31 "
42	34	0.4 "	24 "	trace

Remarks: The above course of treatment was begun after a two months' rest. The first three injections were given two weeks apart and the last three a month apart.

CEREBROSPINAL SYPHILIS: M. W., male, age 42, came to the Clinic for lupus vulgaris; syphilis discovered during examination.

Physical examination: Pupils unequal, irregular and sluggish to light. All deep reflexes very active, more so on right side. Other findings referable to nervous system negative.

Serology:	Blood	9/11/20	+++
		5/ 5/22	negative
	Spinal Fluid	9/11/20	Cells 3 Glob. trace Wass. ++++ with 1.0 c.c. Gold Sol: Luetic curve
		5/ 5/22	Cells 3 Glob. trace Wass. negative with 2.0 c.c. Gold Sol: Negative

Results: Patient has always been asymptomatic as far as nervous system was concerned. His fluid became negative under treatment.

Treatment and Arsenic Determinations:

PREVIOUS NO. I. V. INJECTIONS	PREVIOUS NO. I. S. INJECTIONS	DOSE	INTERVAL AFTER I. V.	AS PER 100 GM. DRIED SPEC.
39	2	0.4 gm.	48 hours	5.6 mg.
40	3	0.4 “	48 “	2.9 “
41	4	0.4 “	48 “	26.5 “
42	5	0.4 “	48 “	.55 “
43	6	0.4 “	24 “	1.3 “
44	7	0.4 “	48 “	.35 “
45	8	0.4 “	48 “	1.12 “
46	9	0.4 “	48 “	5.9 “
49	14	0.4 “	48 “	0. “
50	15	0.4 “	48 “	11.03 “
51	16	0.4 “	72 “	1.24 “
52	17	0.4 “	48 “	trace
53	18	0.4 “	48 “	6.06 “
55	20	0.4 “	48 “	3.78 “

Remarks: The first four intraspinal injections were taken every two weeks; the next four at two to five week intervals. Then followed a rest of two and one-half months when six more were received two to four weeks apart. Another rest of two and one-half months was given when the treatments were resumed three to ten weeks apart.

CEREBROSPINAL SYPHILIS: Wyde., male, age 40, chancre in 1905; no secondaries; complained of headaches.

Physical examination: Pupils unequal, right fixed to light and accommoda tion, left reacts; vision 20/20 both eyes; all the deep reflexes present and active. Other findings negative.

Serology:	Blood	3/ 1/21	++++
		2/28/22	negative
	Spinal Fluid	3/ 1/21	Cells 6 Glob. negative Wass. ++++ to 0.4 c.c. Gold Sol: Luetic curve
		2/28/22	Cells 0 Glob. trace Wass. ++++ to 0.6 c.c. Gold Sol: Luetic curve

Results: Headaches disappeared under treatment. No other changes in physical findings. Fluid now almost negative.

Treatment and Arsenic Determinations:

PREVIOUS NO. I. V. INJECTIONS	PREVIOUS NO. I. S. INJECTIONS	DOSE	INTERVAL AFTER I. V.	AS PER 100 GM. DRIED SPEC.
10	1	0.4 gm.	24 hours	4.19 mg.
11	2	0.4 "	48 "	1.37 "
13	3	0.4 "	48 "	3.51 "
15	5	0.4 "	24 "	11.4 "
17	7	0.4 "	24 "	18.3 "
18	8	0.4 "	24 "	4.44 "
19	9	0.4 "	24 "	0. "
21	11	0.4 "	48 "	5.84 "
22	12	0.4 "	48 "	3.93 "
23	13	0.4 "	48 "	trace

Remarks: At the time the highest values appeared the patient was receiving intravenous salvarsan weekly and intraspinal injections two and three weeks apart. Where zero and trace occurred the intervals for both kinds of treatment had been lengthened to one month.

PARESIS: Sil., male, age 40, infection 12 years ago. Details of history not obtained owing to patient's mental condition.

Physical examination: Pupils, right very much larger than left, both irregular and fixed to light. All deep reflexes very active especially on left side; judgment and memory very poor; marked speech disturbance; tremor; mental depression.

Serology: Blood	5/ 3/17	++++
	5/10/21	negative
Spinal Fluid	5/ 3/17	Cells 57
		Glob. ++
		Wass. ++ with 0.2 c.c.
		Gold Sol: Paretic curve
	5/10/21	Cells 3
		Glob. ++
		Wass. ++ with 0.2 c.c.
		Gold Sol: Paretic curve

Results: Patient was a typical paretic when he came to the Clinic and has shown little change under treatment. He is very slowly deteriorating.

Treatment and Arsenic Determinations:

PREVIOUS NO. I. V. INJECTIONS	PREVIOUS NO. I. S. INJECTIONS	DOSE	INTERVAL AFTER I. V.	AS PER 100 GM. DRIED SPEC.
34	10	0.4 gm.	24 hours	0.54 mg.
36	11	0.4 "	48 "	trace
38	12	0.4 "	72 "	0.29 "
39	13	0.4 "	24 "	2.188 "
42	14	0.4 "	24 "	4.14 "

Remarks: The average intervals were three weeks; some a few days more, some less.

CEREBROSPINAL SYPHILIS: E. B., male, age 49, chancre in 1902; no secondaries; inadequate treatment; chief complaint pains in legs.

Physical examination: Pupils equal and react to light; all the deep reflexes are present, the patellar and ankle jerks being very sluggish. Otherwise findings all negative.

Serology:	Blood	5/ 7/19	++++
		8/23/21	negative
	Spinal Fluid:	5/ 7/19	Cells 213
			Glob. ++++
			Wass. ++++ to 0.2 c.c.
			Gold Sol: Paretic curve
		8/23/21	Cells 2
			Glob. ++
			Wass. +++ with 0.6 c.c.
			Gold Sol: Luetic curve

Results: Still complains of attacks of burning in thighs and calves. His spinal fluid is now completely negative.

Treatment and Arsenic Determinations:

PREVIOUS NO. I. V. INJECTIONS	PREVIOUS NO. I. S. INJECTIONS	DOSE	INTERVAL AFTER I. V.	AS PER 100 GM. DRIED SPEC.
38	14	0.4 gm.	24 hours	trace
39	15	0.4 "	24 "	1.05 mg.
40	16	0.4 "	24 "	4.04 "
41	17	0.4 "	24 "	0. "
42	18	0.4 "	24 "	1.34 "

Remarks: The above treatments were taken very irregularly, intervals of six weeks to three months and longer elapsing between injections.

TABES: Fud., male, age 36, chancre in 1912; secondaries denied. Came to the Clinic complaining of pains in legs, difficulty in walking and incontinence of urine.

Physical examination: Argyll-Robertson pupils; knee and ankle jerks absent; upper deep reflexes very sluggish; Rhomberg; incoordination arms and legs; marked ataxia; sensory disturbance chest and lower extremities.

Serology:	Blood	2/13/20	++++
		5/10/21	negative
	Spinal Fluid	2/13/20	Cells 8
			Glob. +
			Wass. ++++ to 0.4 c.c.
			Gold Sol: Luetic curve
		5/10/21	Cells 2
			Glob. trace
			Wass. ++++ to 1.0 c.c.
			Gold Sol: Luetic curve

Results: Patient's general health has markedly improved. Has pains only occasionally, ataxia is less marked and he has less difficulty in getting about.

Treatment and Arsenic Determinations:

PREVIOUS NO. I. V. INJECTIONS	PREVIOUS NO. I. S. INJECTIONS	DOSE	INTERVAL AFTER I. V.	AS PER 100 GM. DRIED SPEC.
24	10	0.4 gm.	24 hours	4.73 mg.
25	11	0.4 "	24 "	1.08 "
26	12	0.4 "	24 "	16.6 "
27	13	0.4 "	24 "	3.66 "
28	14	0.4 "	24 "	1.37 "
29	15	0.4 "	24 "	1.26 "

Remarks: The average intervals between treatment was three weeks; that preceding the high value 16.6 mg. was 18 days.

TABES: M. T., female, age 51, chancre in 1890 with secondaries. For several years had had "rheumatic" pains in legs and dizziness.

Physical examination: Pupils Argyll-Robertson; upper deep reflexes more active on right side; patellar and Achilles jerks absent; slight sensory disturbance right leg and foot.

Serology:	Blood	8/ 2/20	negative
		8/ 3/22	negative
	Spinal Fluid	8/ 2/20	Cells 10 Glob. + Wass. ++++ to 0.4 c.c. Gold Sol: Luetic curve
		8/ 3/22	Cells 2 Glob. negative Wass. negative Gold Sol: Negative

Results: Patient states health is better than it has been in years, no more attacks of dizziness or pains; physical findings remain as above; spinal fluid negative.

Treatment and Arsenic Determinations:

PREVIOUS NO. I. V. INJECTIONS	PREVIOUS NO. I. S. INJECTIONS	DOSE	INTERVAL AFTER I. V.	AS PER 100 GM. DRIED SPEC.
9	1	0.4 gm.	24 hours	2.0 mg.
10	2	0.4 "	24 "	10.8 "
11	3	0.4 "	24 "	4.0 "
12	4	0.4 "	24 "	0. "
13	5	0.4 "	24 "	4.30 "
14	6	0.4 "	24 "	2.20 "
15	7	0.4 "	24 "	4.70 "
16	8	0.4 "	24 "	8.87 "
17	9	0.4 "	24 "	trace
19	11	0.4 "	48 "	3.43 "
24	16	0.4 "	48 "	0.703 "

Remarks: The first six combined treatments were given at two week intervals followed by a rest period of two months. The next four at intervals of two to five weeks with a four months' rest; the eleventh to sixteenth were again taken at two week intervals.

Cerebrospinal syphilis: N. L., male, age 28, chancre and rash in 1917 for which he took 8 injections of salvarsan and some mercury intramuscularly and by inunction. Came to the Clinic for a blood test.

Physical examination: Practically negative; his deep reflexes were present; pupils reacted to light.

Serology: Blood	2/ 8/22	negative
	2/19/22	negative
Spinal Fluid:	4/19/22	Cells 20
		Glob. +++
		Wass. ++++ to 1.0 c.c.
		Gold Sol: Luetic curve
	4/19/22	Cells negative
		Glob. trace
		Wass. +++ with 2.0 c.c.
		Gold Sol: Luetic curve

Results: No symptoms developed during treatment and fluid rapidly changed to negative.

Treatment and Arsenic Determinations:

PREVIOUS NO. I. V. INJECTIONS	PREVIOUS NO. I. S. INJECTIONS	DOSE	INTERVAL AFTER I. V.	AS PER 100 GM. DRIED SPEC.
9	1 dr. 1 SE	0.4 gm.	48 hours	trace
10	1 dr. 2 SE	0.4 "	48 "	4.8 mg.
11	1 dr. 3 SE	0.4 "	48 "	2.82 "
12	1 dr. 4 SE	0.4 "	48 "	2.36 "
13	1 dr. 5 SE	0.4 "	48 "	15.3 "
14	1 dr. 6 SE	0.4 "	48 "	1.07 "
15	1 dr. 7 SE	0.4 "	48 "	trace

Remarks: The above treatments were given at two week intervals.

Cerebrospinal syphilis: G. W., male, age 43, chancre in 1909 with a rash and headache. Took a course of mercury intramuscularly. In 1919 received 15 injections of salvarsan and 30 of mercury. Had no complaints except occasional headaches.

Physical examination: Pupils slightly irregular, unequal and sluggish to light; upper deep reflexes active and equal; patellar and ankle jerks very active and unequal; all other findings negative.

Serology:	Blood	2/10/21	++++
		4/ 5/22	+++
	Spinal Fluid	2/10/21	Cells 8 Glob. ++ Wass. ++++ to 0.2 c.c. Gold Sol: Luetic curve
		4/ 5/22	Cells 0 Glob. trace Wass. ++++ with 1.5 c.c. Gold Sol: Luetic curve

Results: Under persistent treatment the laboratory findings diminished in strength; he no longer suffered from headaches and no further developments occurred.

Treatment and Arsenic Determinations:

PREVIOUS NO. I. V. INJECTIONS	PREVIOUS NO. I. S. INJECTIONS	DOSE	INTERVAL AFTER I. V.	AS PER 100 GM. DRIED SPEC.
1	1	0.4 gm.	48 hours	4.8 mg.
3	3	0.4 “	48 “	0.0581 “
4	4	0.4 “	48 “	trace
5	5	0.4 “	48 “	trace
6	6	0.4 “	48 “	1.30 “
7	7	0.4 “	48 “	7.68 “
10	10	0.4 “	48 “	trace
12	12	0.4 “	48 “	0. “
13	13	0.4 “	48 “	0.67 “
14	14	0.4 “	48 “	6.2 “
15	15	0.4 “	48 “	1.2 “
16	16	0.4 “	48 “	0. “
18	18	0.4 “	48 “	trace
21	19	0.4 “	48 “	1.45 “
22	20	0.4 “	48 “	7.10 “
23	21	0.4 “	48 “	0.6702 “
24	22	0.4 “	48 “	trace
25	23	0.4 “	48 “	4.51 “

Remarks: The first eight intravenous and intraspinal injections were taken at two week intervals followed by a three months' rest. The succeeding ones were given in courses of six injections at two week intervals with rest periods of three to three and one-half months. The highest values in this patient appeared at the end of each course.

TABES: J. K., age 28, chancre in 1910; secondaries denied. Had local treatment only at time of infection. Between 1914 and 1915 received 32 injections of salvarsan; no mercury. Came for advice because his Wassermann remained positive. Complained of occasional twinges of pain in his extremities.

Physical examination: Pupils were unequal, fundus normal; vision 20/20 both eyes. His reflexes in the upper extremities were equal and active. One knee jerk was absent as well as both ankle jerks; other findings negative.

Serology:	Blood	9/13/17	+
		12/29/22	++++
	Spinal Fluid	9/13/17	Cells 7
			Glob. ++++
			Wass. ++++ to 0.4 c.c.
			Gold Sol: Luetic curve
		12/29/22	Cells 5
			Glob. ++
			Wass. ++++ with 0.6 c.c.
			Gold Sol: Paretic curve

Results: Under prolonged treatment his blood was negative for nearly two years. It then became and remained positive. His spinal fluid by May 3rd, 1919, was reduced to ++ with 1.5 c.c. It remained positive with this amount until March, 1922. He was urged to take six months' rest from all therapy, but instead went to a private physician and had 18 injections of neosalvarsan. When he returned in October, 1922, his fluid was positive with 0.6 c.c. and gave a paretic curve. It next showed ++++ with 0.2 c.c. and continued so with a paretic curve until the last examination on April 5th, 1923. It was noted during the past months that he became very irritable at times. Beyond this and an extreme apprehensiveness regarding his condition and reluctance to follow advice relative to rest from treatment no mental abnormalities were noted. Two weeks ago he complained of feeling ill and after a few days went to a hospital where a diagnosis of typhoid fever was made. He died on May 12, 1923.

Treatment and arsenic determinations:

PREVIOUS NO. I. V. INJECTIONS	PREVIOUS NO. I. S. INJECTIONS	DOSE	INTERVAL AFTER I. V.	AS PER 100 GM. DRIED SPEC.
78	40	0.4 gm.	48 hours	5.13 mg.
79	41	0.4 “	48 “	0. “
80	42	0.4 “	48 “	trace
81	43	0.4 “	48 “	0. “
82	44	0.4 “	48 “	4.13 “
84	46	0.4 “	48 “	21.2 “
85	47	0.4 “	48 “	2.10 “
86	48	0.4 “	48 “	1.15 “
87	49	0.4 “	48 “	4.41 “
96	50	0.4 “	48 “	13.5 “
97	51	0.4 “	48 “	3.08 “

Remarks: The first examination showing 5.13 mg. metallic arsenic was made 48 hours after an intravenous injection following a four months' rest from all treatment. The next four treatments were taken two weeks apart, then a month elapsed before the examination showing 21.2 mg. The succeeding three treatments were two weeks apart. The cerebrospinal fluid showing 13.5 mg. was taken eight months after the last intraspinal injection, he having received, however, in the meantime eighteen intravenous injections of neosalvarsan from an outside physician.

EXPLANATION OF ABBREVIATIONS USED IN TABLES:

I. V. = Intravenous injection
I. S. = Intraspinal injection
Dr. = Drainage
S. E. = Swift-Ellis method of intraspinal treatment
S. F. = Spinal Fluid
S.; Sal.; Salv. = Salvarsan
S. S. = Silver Salvarsan
Neo. = Neosalvarsan
Glob. = Globulin
Wass. = Wassermann
I = Primary Syphilis
II = Secondary Syphilis
III = Tertiary Syphilis
C. S. L. = Cerebro-spinal syphilis
G. P. = General paresis

Table I

Spinal Fluid Findings After the Use of Salvarsan in the Swift-Ellis Method of Treatment

PATIENT	SERIAL NO.	NO. PREVIOUS I. V. INJEC.	NO. PREVIOUS I. S. INJEC.	DOSE OF DRUG (SAL.)	WT. OF SPECIMEN		PER CENT SOLIDS	AS. IN MG. PER 100 GMS. DRIED SPEC.	AGE	SEX AND COLOR	SPINAL FLUID FINDINGS				BLOOD WASS.	DURATION OF INFECTION	DIAGNOSIS AND REMARKS
					MOIST	DRY					CELLS	GLOB.	WASSERMANN	GOLD SOL			
Secondary Syphilis Interval 2 Hours (1 Case)																	
A. A.	437	16	2 S. E.	0.4	5.0122	0.543	1.08	11.0	22	F. W.	2	Trace	Neg. 2 c.c.	0000000000	Neg.	2 yr.	Meningitis. Chancre of lip. 4 mos. later, headaches, ocular palsies; positive fluid
Interval 24 Hours (1 Case)																	
J. B.	254	18	9 Dr. 4 S. E.	0.4	13.5540	0.1478	1.08	4.7	28	M. W.	10	+	+++ 0.6 c.c.	5555431000	+++	2 yr.	Meningo-encephalitis; 4 mos. after infection bilateral facial palsy with strongly + fluid
Interval 48 Hours (6 Cases)																	
J. B.	39	17	9 Dr. 3 S. E.	0.4	13.2986	0.1436	1.07	6.9	28	M. W.	6	+	++++ 0.4 c.c.	5555431000	Neg.	2 yr.	Meningo-encephalitis; 4 mos. after infection bilateral facial palsy with strongly + fluid
J. B.	328	19	9 Dr. 5 S. E.	0.4	4.7992	0.0575	1.19	0	28	M. W.	6	+	+++ 0.6 c.c.	5555431000	Neg.	2 yr.	
J. B.	366	21	9 Dr. 6 S. E.	0.4	16.0172	0.1618	1.01	1.5	28	M. W.	2	Trace	++++ 1.0 c.c.	1233100000	Neg.	2 yr.	
J. B.	428	23	9 Dr. 8 S. E.	0.4	8.6151	0.0882	1.02	Trace	28	M. W.	2	Trace	++++ 1.0 c.c.	1233100000	Neg.	2 yr.	
J. B.	455	24	9 Dr. 9 S. E.	0.4	15.8530	0.1549	0.98	0.64	28	M. W.	3	Trace	++++ 1.0 c.c.	1233100000	Neg.	2 yr.	
J L	176	27	6 S. E.	0.4	5.0458	0.0431	0.85	11.6	25	M. W.	3	Trace	Neg. 2.0 c.c.	0000000000	Neg.	1 yr.	Meningitis. 6 mos. after infection routine puncture strongly positive; asymptomatic
Interval 72 Hours (1 Case)																	
S. A.	1761	29	7 S. E.	0.4	5.6140	0.0601	1.07	4.98	25	F. W.	0	Trace	+++ 0.6 c.c.	1122100000	Neg.	2 yr.	Meningitis. 6 mos. after infection fluid strongly +; asymptomatic
Tertiary Syphilis Interval 30 Minutes (2 Cases)																	
J. M.	987	5	5 S. E.	0.3	4.9223	0.0481	0.97	4.1	34	M. W.	2	Neg.	++++ 0.4 c.c.	1233210000	+++	10 yr.	C. S. L.; now negative
D. D.	1526	12	3 S. E.	0.4	5.5505	0.0569	1.02	0	39	M. W.	2	++	+++ 0.8 c.c.	2233210000	++++	8 yr.	C. S. L. asymptomatic

TABLE I—Cont'd

TERTIARY SYPHILIS—Cont'd

INTERVAL 1 HOUR (2 CASES)																	
C. B.	508	11	1 Dr. 2 S. E.	0.4	14.5106	0.1532	1.05	2.29	42	M. W.	10	++	++++ 0.2 c.c.	5555543100	++++	20 yr.	G. P. and Optic atrophy; In Institution.
J. McN.	970	16	7 S. E.	0.4	6.0776	0.0651	1.07	0.76	34	M. W.	2	Trace	++++ 0.6 c.c.	1233210000	++++	11 yr.	Tabes
INTERVAL 2 HOURS (15 CASES)																	
C. B.	600	12	1 Dr. 3 S. E.	0.4	13.8177	0.1636	1.18	0.61	42	M. W.	8	+++	++++ 0.2 c.c.	5555543100	++++	20 yr.	G. P. and Optic atrophy; in Institution.
C. B.	833	14	1 Dr. 5 S. E.	0.4	11.9286	0.1275	1.06	6.27	42	M. W.	10	++	++++ 0.2 c.c.	5555543100	++++	20 yr.	G. P. and Optic atrophy; in Institution.
W. C.	507	5	3 S. E.	0.4	13.9844	0.1738	1.24	0.575	42	M. W.	48	++++	++++ 0. 2. c.c.	5555543100	++++	23 yr.	G. P. Now in Institution
D. D.	2878	21	14 S. E.	0.4	4.9105	0.0633	1.28	18.9	39	M. W.	4	++	++++ 2.0 c.c.	2233210000	++++	8 yr.	C. S. L.
J. G.	329	22	1 S. E.	0.4	4.8552	0.0472	0.97	1.06	29	M. W.	9	+++	++++ 0.1 c.c.	1233210000	++++	9 yr.	C. S. L. asymptomatic
J. M.	1002	7	7 S. E.	0.3	7.5580	0.0745	0.98	1.32	34	M. W.	3	Neg.	++++ 1.0 c.c.	1233210000	+++		C. S. L. now negative
J. M.	1884	11	11 S. E.	0.4	7.4201	0.0806	1.08	2.48	34	M. W.	2	Trace	++++ 1.0 c.c.	1233210000	+++	10 yr.	C. S. L. now negative
E. E.	1513	15	3 S. E.	0.4	13.2765	0.1419	1.06	1.76	34	M. B.	12	++++	++++ 0. 4. cc..	2233210000	++++	9 yr.	Optic atrophy
C. H.	463	16	1 S. E.	0.3	14.5241	0.1512	1.06	0.32	42	M. W.	10	++++	++++ 0.1 c.c.	5555543100	++++	4 yr.	Tabo-paresis. Died in Institution
J. McN.	491	10	1 S. E.	0.4	14.8460	0.1641	1.10	0	34	M. W.	5	++	++++ 0.4 c.c.	1223321000	++++	11 yr.	Tabes
S. M.	235	25	8 S. E.	0.4	14.3584	0.1557	1.08	9.09	42	M. W.	2	Neg.	++++ 0.6 c.c.	1122100000	++++	16 yr.	Early tabes
S. M.	257	26	9 S. E.	0.4	13.3220	0.1367	1.02	13.1	42	M. W.	2	Neg.	++++ 0.6 c.c.	1122100000	++++	16 yr.	Early tabes
S. M.	509	28	11 S. E.	0.4	7.0963	0.0700	0.98	5.0	42	M. W.	4	Neg.	++++ 0.6 c.c.	1122100000	++++	16 yr.	Early tabes
S. M.	954	30	13 S. E.	0.4	5.6821	0.0586	1.03	Trace	42	M. W.	3	Neg.	++++ 0.6 c.c.	1122100000	++++	16 yr.	Early tabes
S M.	852	31	14 S. E.	0.4	14.7486	0.1438	0.97	1.7	42	M. W.	1	Neg.	++++ 0.6 c.c.	1122100000	++++	16 yr.	Early tabes
INTERVAL 3 HOURS (4 CASES)																	
C. O. S.	2349	22	3 S. E.	0.4	12.1315	0.1263	1.04	2.37	32	M. W.	8	++	++++ 0.2 c.c.	5555431000	++++		G. P.; clinical manifestations
E. A.	582	44	12 S. E.	0.4	13.7811	0.1395	1.01	Trace	29	M. W.	10	++	++++ 0.2 c.c.	5554310000	Neg.	9 yr.	Meningo-vasculitis
P. A. T.	584	7	6 S. E.	0.4	5.6528	0.0591	1.04	0.846	46	M. W.	6	++	++++ 0.4 c.c.	5555431000	++++	24 yr.	Optic atrophy
S. M.	652	29	12 S. E.	0.4	15.0042	0.1477	0.98	Trace	42	M. W.	2	Trace	++++ 0.6 c.c.	1233210000	++++	16 yr	Early tabes
INTERVAL 4 HOURS (2 CASES)																	
W. C.	578	6	4 S. E.	0.4	14.1896	0.1512	1.06	3.30	42	M. W.	12	++++	++++ 0.2 c.c.	5555543100	++++	23 yr.	G. P.; clinical manifestations
P. A. T.	580	6	5 S. E.	0.4	6.3589	0.0683	1.07	58.5	46	M. W.	8	++	++++ 0.4 c.c.	5555431000	++++	24 yr.	Optic atrophy (complete)
INTERVAL 24 HOURS (84 CASES)																	
A. M.	401	16	2 S. E.	0.4	14.9660	0.1527	1.02	0.65	37	M. W.	4	Trace	+++ 0.4 c.c.	4444332100	Neg.	7 yr	C. S. L
C. H.	2711	3	1 S. E.	0.4	10.3575	0.1166	1.12	Trace	36	M. W.	10	++++	++++ 2.0 c.c.	1233210000	++++	17 yr.	C. S. L.
F. A.	164	15	9 S. E.	0.4	3.4732	0.0431	1.24	34.9	34	M. W.	3	Neg.	+++ 0.8 c.c.	1121000000	++++	9 yr.	C. S. L.; clinical symptoms
C. G.	245	54	34 S. E.	0.4	6.1182	0.0639	1.04	17.2	35	M. W.	2	Trace	+++ 0.8 c.c.	1233210000	Neg.	14 yr.	C. S. L.; clinical manifestations
C. G.	346	55	35 S. E.	0.4	10.9041	0.1291	1.18	0.79	35	M. W.	1	Trace	+++ 0.8 c.c.	1233210000	Neg.	14 yr.	C. S. L.; clinical manifestations
C. G.	363	56	36 S. E.	0.4	3.3577	0.0348	1.03	2.9	35	M. W.	4	Trace	+++ 0.8 c.c.	1233210000	Neg.	14 yr.	C. S. L.; clinical manifestations
C. G.	405	58	37 S. E.	0.4	6.8485	0.0737	1.07	3.40	35	M. W.	0	Trace	++++ 1.0 c.c.	1233210000	Neg.	14 yr.	C. S. L.: clinical manifestations
C. G.	654	63	38 S. E.	0.4	12.6701	0.1311	1.03	0	35	M. W.	3	Trace	++++ 1.0 c.c.	1233210000	Neg.	14 yr.	C. S. L.; clinical manifestations
C. G.	700	64	39 S. E.	0.4	10.5741	0.1091	1.03	1.83	35	M. W.	0	Neg.	++++ 1.5 c.c.	1233210000	Neg.	14 yr.	C. S. L.; clinical manifestations
C. G.	702	65	40 S. E.	0.4	15.5193	0.1627	1.04	2.04	35	M. W.	Neg.	Neg.	++++ 0.4 c.c.	1233210000	Neg.	14 yr.	C. S. L.; clinical manifestations

TABLE I—Cont'd
TERTIARY SYPHILIS—Cont'd
INTERVAL 24 HOURS—Cont'd

PATIENT	SERIAL NO.	NO. PREVIOUS I. V. INJEC.	NO. PREVIOUS I. S. INJEC.	DOSE OF DRUG (SAL.)	WT. OF SPECIMEN		PER CENT SOLIDS	AS. IN MG. PER 100 GMS. DRIED SPEC.	AGE	SEX AND COLOR	SPINAL FLUID FINDINGS				BLOOD WASS.	DURATION OF INFECTION	DIAGNOSIS AND REMARKS
					MOIST	DRY					CELLS	GLOB.	WASSERMANN	GOLD SOL			
C. G.	1230	66	41 S. E.	0.4	6.0073	0.0621	1.03	12.0	35	M. W.	0	Neg.	++++ 1.5 c.c.	1233210000	Neg.	14 yr.	C. S. L.; clinical manifestations
E K.	117	6	1 S. E.	0.3	14.7417	0.1511	1.02	2.64	32	F. W.	10	+	++++ 0.2 c.c.	1233210000	Neg.		C. S. L.; clinical symptoms
E. K.	172	7	2 S. E.	0.3	15.7878	0.1683	1.04	8.47	32	F. W.	7	++	++++ 0.2 c.c.	1233210000	Neg.		C. S. L.; clinical symptoms
E K.	331	9	4 S. E.	0.3	5.9986	0.0591	0.98	6.90	32	F. W.	4	++	++++ 0.6 c.c.	1233210000	Neg.		C. S. L.; clinical symptoms
E. K.	461	11	6 S. E.	0.3	11.8431	0.1163	0.98	4.30	32	F. W.	5	++	++++ 0.6 c.c.	1233210000	Neg.		C. S. L.; clinical symptoms
E. K.	517	12	7 S. E.	0.3	13.5074	0.1336	0.98	Trace	32	F. W.	4	++	++++ 0.6 c.c.	1233210000	Neg.		C. S. L.; clinical symptoms
J. M.	889	3	3 S. E.	0.3	12.7171	0.1310	1.03	3.05	34	M. W.	3	+	++++ 0.4 c.c.	1233210000	++++	12 yr.	C. S. L.; clinical symptoms
J. M.	1170	9	9 S. E.	0.3	6.4150	0.0684	1.06	2.9	34	M. W.	Neg.	Neg.	++++ 0.6 c.c.	1233210000	++	12 yr.	C. S. L.; clinical symptoms
J. M.	1269	10	10 S. E.	0.3	6.4414	0.0687	1.07	23.0	34	M. W.	Neg.	Neg.	++++ 0.6 c.c.	1233210000	++	12 yr.	C. S. L.; clinical symptoms
L. V.	8	36	29 S. E.	0.4	9.6040	0.0963	1.00	8.00	35	M. W.	3	++	++++ 0.4 c.c.	1233321000	+	14 yr.	C. S. L.; ocular palsy
L. V.	64	37	30 S. E.	0.4	5.4424	0.0749	1.37	20.0	35	M. W.	4	++	++++ 0.4 c.c.	1233321000	+	14 yr.	C. S. L.; ocular palsy
L. V.	115	38	31 S. E.	0.4	12.4384	0.1274	1.02	7.90	35	M. W.	0	+	++++ 0.4 c.c.	1233321000	+	14 yr.	C. S. L.; ocular palsy
L. V.	205	39	32 S. E.	0.4	12.3851	0.1393	1.12	23.90	35	M. W.	2	+	++++ 0.4 c.c.	1233321000	+	14 yr.	C. S. L.; ocular palsy
L. V.	419	42	34 S. E.	0.4	14.5732	0.1449	0.99	Trace	35	M. W.	2	Trace	++++ 0.4 c.c.	1233321000	+	14 yr.	C. S. L.; ocular palsy
M. W.	426	43	6 S. E.	0.4	7.1260	0.0748	1.04	1.3	40	M. W.	2	Neg.	++++ 1.0 c.c.	1223100000	Neg.	12 yr.	C. S. L.
M. W.	1282	10	1 S. E.	0.4	15.1546	0.1913	1.26	4.19	40	M. W.	2	Trace	++++ 0.4 c.c.	2233221000	++++	16 yr.	C. S. L.
M. W.	441	15	5 S. E.	0.4	7.9680	0.0914	1.02	11.4	40	M. W.	4	Trace	++++ 0.4 c.c.	2233221000	++++	16 yr.	C. S. L.
M. W.	910	17	7 S. E.	0.4	8.7110	0.0908	1.04	18.3	40	M. W.	2	Trace	++++ 0.6 c.c.	2233221000	++++	16 yr.	C. S. L.
M. W.	1093	18	8 S. E.	0.4	7.7330	0.0843	1.09	4.44	40	M. W.	2	Trace	++++ 0.8 c.c.	2233221000	++++	16 yr.	C. S. L.
M. W.	1488	19	9 S. E.	0.4	5.7156	0.0574	1.004	0	40	M. W.	2	Trace	++++ 0.6 c.c.	2233221000	++++	16 yr.	C. S. L.
W. C.	506	5	2 S. E.	0.4	14.7784	0.1701	1.15	19.6	42	M. W.	20	++++	++++ 0.2 c.c.	5555543100	++++	23 yr.	G. P.; clinical manifestations
C. O. S.	48	6	1 S. E.	0.4	6.7435	0.0756	1.12	0.66	32	M. W.	1	++++	++++ 0.1 c.c.	5555431000	++++	11 yr.	G. P.; clinical manifestations
C. O. S.	158	8	2 S. E.	0.4	11.9892	0.2049	1.70	4.05	32	M. W.	10	++++	++++ 0.2 c.c.	5555431000	++++	11 yr.	G. P.; clinical manifestations
R. O. S.	722	12	1 S. E.	0.4	9.6091	0.1101	1.14	0.467	48	M. W.	18	++++	++++ 0.4 c.c.	5433100000	++++	29 yr.	G. P.; active
S. I. L.	361	34	10 S. E.	0.4	7.9224	0.0916	1.15	0.54	27	M. W.	8	++	++ 0.2 c.c.	5555542100	+	10 yr.	G. P.; clinical manifestations
S. I. L.	503	39	13 S. E.	0.4	14.8396	0.1599	1.07	2.188	27	M. W.	4	++	++ 0.2 c.c.	5555542100	+	10 yr.	G. P.; clinical manifestations
S. I. L.	519	42	14 S. E.	0.4	14.9258	0.1608	1.07	4.14	27	M. W.	3	++	++ 0.2 c.c	5555542100	+	10 yr.	G. P.; clinical manifestations
J. R.	157	25	8 S. E.	0.4	11.7626	0.1364	1.15	11.7	39	M. W.	2	Trace	Neg. 2.0 c.c.	0000000000	Neg.	5 yr.	Meningitis, asymptomatic. Routine puncture yr. after infection, strongly +
J. R.	467	27	9 S. E.	0.4	5.2111	0.0521	0.99	38.3	39	M. W.	2	Neg.	Neg. 2.0 c.c.	0000000000	Neg.	5 yr.	Meningitis, asymptomatic. Routine puncture yr. after infection, strongly +
J. R.	1229	29	11 S. E.	0.4	7.8955	0.0821	1.04	1.21	39	M. W.	0	Neg	Neg. 2.0 c.c.	0000000000	Neg.	5 yr.	Meningitis, asymptomatic. Routine puncture yr. after infection, strongly +
E. A.	521	42	11 S. E.	0.4	13.7539	0.1360	0.98	2.2	29	M. W.	10	++	++++ 0.2 c.c.	5554310000	++++	9 yr.	Meningo - Vasculitis
E. B.	357	38	14 S. E.	0.4	6.1206	0.0674	1.10	Trace	49	M. W.	0	++	+++ 0.6 c.c.	5555431000	Neg.	19 yr.	Meningo - Vasculitis. Fluid was strongly positive
E. B.	442	39	15 S. E.	0.4	8.2033	0.0948	1.15	1.05	49	M. W.	0	++	+++ 0.6 c.c.	5555431000	Neg.	19 yr.	Meningo - Vasculitis. Fluid was strongly positive
E. B.	516	40	16 S. E.	0.4	6.9630	0.0742	1.06	4.04	49	M. W.	3	++	+++ 0.6 c.c.	5555431000	Neg.	19 yr.	Meningo - Vasculitis. Fluid was strongly positive
E. B.	538	41	17 S. E.	0.4	6.8777	0.0770	1.12	0	49	M. W.	2	++	+++ 0.6 c.c.	5555431000	Neg.	19 yr	Meningo - Vasculitis. Fluid was strongly positive
E. B.	701	42	18 S. E.	0.4	13.8744	0.1494	1.07	1.34	49	M. W.	2	++	+++ 0.6 c.c.	5555431000	Neg.	19 yr.	Meningo - Vasculitis. Fluid was strongly positive
E E.	1376	14	1 S. E.	0.4	11.4230	0.1530	1.43	3.9	34	M. B.	15	++++	++++ 0.4 c.c.	2233210000	++++	11 yr.	Optic atrophy

TABLE I—Cont'd

TERTIARY SYPHILIS—Cont'd

INTERVAL 24 HOURS—Cont'd

E. E.	1760	17	4 S. E.	0.4	6.1821	0.0722	1.16	0	34	M. B.	8	++++	++++ 0.4 c.c.	1123210000	++++	11 yr.	Optic atrophy
P. A. T.	505	5	5 S. E.	0.4	13.3482	0.1391	1.04	2.16	46	M. W.	10	++++	++++ 0.4 c.c.	5555431000	++++	24 yr.	Optic atrophy
C. L.	464	8	1 S. E.	0.4	13.1516	0.1356	1.038	Trace	49	M. W.	0	Neg.	Neg.	0000000000	Neg.	25 yr.	Tabes (abortive)
C. L.	518	9	2 S. E.	0.4	15.7100	0.1658	1.05	6.03	49	M. W.	0	Neg.	Neg.	0000000000	Neg.	25 yr.	Tabes (abortive)
M. C.	767	19	2 S. E.	0.4	7.7892	0.0821	1.06	Trace	37	F. W.	0	Neg.	Neg.	0000000000	Neg.	8 yr.	Tabes (abortive)
F. E.	459	18	1 S. E.	0.4	6.4900	0.0697	1.07	0	49	M. W.	4	Trace	++++ 0.4 c.c.	1223210000	Neg.	12 yr.	Tabes (active)
F. N. D.	66	24	10 S. E.	0.4	11.8516	0.1270	1.07	4.73	36	M. W.	0	Trace	++ 0.6 c.c.	1123210000	Neg.	9 yr.	Tabes. Had strongly + fluid before treatment. Degenerative type.
F. N. D.	171	25	11 S. E.	0.4	12.4435	0.1382	1.11	1.08	36	M. W.	3	Neg.	Neg.	1123210000	Neg.	9 yr.	Tabes. Had strongly + fluid before treatment. Degenerative type.
F. N. D.	244	26	12 S. E.	0.4	4.2254	0.0422	0.99	16.6	36	M. W.	5	Neg.	+++ 0.8 c.c.	1123210000	Neg.	9 yr.	Tabes. Had strongly + fluid before treatment. Degenerative type.
F. N. D.	340	27	13 S. E.	0.4	6.1910	0.0818	1.32	3.66	36	M. W.	3	Neg.	+ 0.8 c.c.	1123210000	Neg.	9 yr.	Tabes. Had strongly + fluid before treatment. Degenerative type.
F. N. D.	382	28	14 S. E.	0.4	7.3436	0.0730	0.99	1.37	36	M. W.	4	Neg.	++++ 1.0 c.c.	1123210000	Neg.	9 yr.	Tabes. Had strongly + fluid before treatment. Degenerative type.
F. N. D.	427	29	15 S. E.	0.4	7.6775	0.0782	1.01	1.26	36	M. W.	2	Trace	++++ 1.0 c.c.	1123210000	Neg.	9 yr.	Tabes. Had strongly + fluid before treatment. Degenerative type.
K. E.	1074	16	5 S. E.	0.4	7.1920	0.0132	1.43	5.8	35	M. W.	20	++	++++ 0.4 c.c.	1233210000	Neg.		Tabes (mild form)
K. E.	1586	24	13 S. E.	0.4	11.3783	0.1183	1.03	2.62	35	M. W.	2	Neg.	Neg.	0000000000	Neg.		Tabes (mild form)
J. E.	1342	3	2 S. E.	0.4	7.9895	0.0810	1.01	7.4		M. W.	10	+	++++ 0.2 c.c.	2233210000	Neg.		Tabes (active)
J. E.	1469	4	3 S. E.	0.4	10.8468	0.1121	1.03	7.13		M. W.	4	++	++++ 0.2 c.c.	2233210000	Neg.		Tabes (active)
J. E.	1668	5	4 S. E.	0.4	6.0689	0.0537	0.88	0		M. W.	4	++	++++ 0.4 c.c.	2233210000	Neg.		Tabes (active)
J. McN.	1851	23	1 Dr. 11 S. E.	0.4	7.5709	0.0806	1.06	6.20	34	M. W.	2	Trace	++++ 0.6 c.c.	1233210000	+	11 yr.	Tabes—clinically positive
J. McN.	583	12	3 S. E.	0.4	11.1414	0.1153	1.03	Trace	34	M. W.	5	++	++++ 0.4 c.c.	1233210000	++++	11 yr.	Tabes—clinically positive
J. McN.	655	14	5 S. E.	0.4	12.5881	0.1465	1.16	Trace	34	M. W.	3	++	++++ 0.4 c.c.	1233210000	++++	11 yr.	Tabes—clinically positive
J. McN.	909	15	6 S. E.	0.4	6.3168	0.0650	1.03	12.3	34	M. W.	2	Trace	++++ 0.6 c.c.	1233210000	++++	11 yr.	Tabes—clinically positive
J. McN.	1030	18	8 S. E.	0.4	7.3866	0.0786	1.06	0	34	M. W.	4	Trace	++++ 0.8 c.c.	1233210000	++++	11 yr.	Tabes—clinically positive
McL.	9	9	3 S. E.	0.4	7.332	0.0845	1.15	4.73	43	M. W.	13	+++	++++ 0.1 c.c.	5544321000	+++		Tabo-paresis
McL.	174	10	4 S. E.	0.4	15.4634	0.1752	1.13	1.9	43	M. W.	8	+++	++++ 0.1 c.c.	5544321000	+++		Tabo-paresis
M. T.	402	9	1 S. E.	0.3	12.7739	0.1245	0.98	2.00	51	F. W.	10	+	++++ 0.4 c.c.	2233210000	Neg.	30 yr.	Tabes (incipient)
M. T.	443	10	2 S. E.	0.3	7.2458	0.0739	1.02	10.8	51	F. W.	8	+	++++ 0.4 c.c.	2233210000	Neg.	30 yr.	Tabes (incipient)
M. T.	510	11	3 S. E.	0.3	7.5721	0.0757	0.99	4.00	51	F. W.	6	+	++++ 0.4 c.c.	2233210000	Neg.	30 yr.	Tabes (incipient)
M. T.	520	12	4 S. E.	0.3	14.4024	0.1397	0.97	0	51	F. W.	0	Neg.	++++ 0.8 c.c.	2233210000	Neg.	30 yr.	Tabes (incipient)
M. T.	657	13	5 S. E.	0.3	6.1115	0.0686	1.12	4.30	51	F. W.	0	Neg.	++++ 0.8 c.c.	2233210000	Neg.	30 yr.	Tabes (incipient)
M. T.	769	14	6 S. E.	0.3	12.6210	0.1265	1.00	2.20	51	F. W.	3	Neg.	++++ 0.8 c.c.	2233210000	Neg.	30 yr.	Tabes (incipient)
M. T.	890	15	7 S. E.	0.3	5.9687	0.0632	1.05	4.70	51	F. W.	2	Neg.	++++ 0.8 c.c.	2233210000	Neg.	30 yr.	Tabes (incipient)
M. T.	953	16	8 S. E.	0.3	7.8171	0.0778	0.99	8.87	51	F. W.	1	Neg.	++++ 0.8 c.c.	2233210000	Neg.	30 yr.	Tabes (incipient)
M. T.	1076	17	9 S. E.	0.3	5.5770	0.0582	1.04	Trace	51	F. W.	0	Neg.	++++ 0.8 c.c.	2233210000	Neg.	30 yr.	Tabes (incipient)
T. U. B.	170	2	1 S. E.	0.2	11.6420	0.1277	1.09	12.5	38	M. W.	10	+	++++ 0.6 c.c.	1233210000	++++	20 yr.	Tabes, and optic atrophy
C. W.	212	29	23 S. E.	0.4	12.9283	0.1412	1.09	5.6	55	M. W.	14	++	++++ 0.6 c.c.	1233210000	Neg.	32 yr.	Tabes
C. W.	460	33	27 S. E.	0.4	12.7314	0.1322	1.03	0	55	M. W.	4	Trace	++++ 0.6 c.c.	1233210000	Neg.	32 yr.	Tabes
B. W.	2518	23	16 S. E.	0.4	11.2451	0.1189	1.05	0.840	39	M. W.	2	+	++++ 2.0 c.c.	1112321000	Neg.	17 yr.	Tabes (had been strongly +)

INTERVAL 48 HOURS (112 CASES)

M. C.	905	20	1 S. E.	0.4	15.1261	0.1458	0.96	4.5	37	F. W.	20	++	++++ 0.6 c.c.	2233210000	++++	8 yr.	C. S. L.
M. C.	952	21	2 S. E.	0.4	6.5365	0.0695	1.06	2.8	37	F. W.	Neg.	Neg.	++++ 1.0 c.c.	2233210000	++++	8 yr.	C. S. L.
F. D.	2883	11	3 S. E.	0.4	10.7665	0.1906	1.01	5.47	23	M. W.			++++ 2.0 c.c.	1232100000	+++		C. S. L.
D. D.	1755	13	3 S. E.	0.4	5.5924	0.0615	1.09	0	39	M. W.	2	++	+++ 0.8 c.c.	5555431000	++++	8 yr.	C. S. L.; asymptomatic
D. D.	2323	21	11 S. E.	0.4	6.2373	0.0694	1.11	1.44	39	M. W.	4	Trace	++++ 0.8 c.c.	123321000	++++	8 yr.	C. S. L.; asymptomatic
E. D.	3014	3	2 S. E.	0.4	4.1477	0.0395	0.95	40.5	31	M. W.	4	++	++++ 0.8 c.c.		+++	7 yr.	C. S. L.; asymptomatic
E. K.	384	10	5 S. E.	0.3	8.3779	0.0856	1.02	3.50	32	F. W.	7	+	++++ 0.6 c.c.	1233210000	Neg.		C. S. L.; clinical symptoms
N. L.	1379	9	1 Dr. 1 S. E.	0.3	8.1200	0.0861	1.06	Trace	24	M. W.	20	+++	++++ 1.0 c.c.	1122100000	Neg.	5 yr.	C. S. L.; clinical symptoms

TABLE I—Cont'd
TERTIARY SYPHILIS—Cont'd
INTERVAL 48 HOURS—Cont'd

PATIENT	SERIAL NO.	NO. PREVIOUS I. V. INJEC.	NO. PREVIOUS I. S. INJEC.	DOSE OF DRUG (SAL.)	WT. OF SPECIMEN		PER CENT SOLIDS	AS. IN MG. PER 100 GMS. DRIED SPEC.	AGE	SEX AND COLOR	SPINAL FLUID FINDINGS				BLOOD WASS.	DURATION OF INFECTION	DIAGNOSIS AND REMARKS
					MOIST	DRY					CELLS	GLOB.	WASSERMANN	GOLD SOL			
N. L.	1424	10	1 Dr. 2 S. E.	0.3	8.1819	0.825	1.08	4.8	24	M. W.	10	Trace	++++ 1.0 c.c.	1122100000	Neg.	5 yr.	C. S. L.; clinical symptoms
N. L.	1527	11	1 Dr. 3 S. E.	0.3	6.6106	0.0707	1.06	2.82	24	M. W.	0	Trace	+++ 2.0 c.c.	1122100000	Neg.	5 yr.	C. S. L.; clinical symptoms
N. L.	1673	12	1 Dr. 4 S. E.	0.3	4.7677	0.0423	0.88	2.36	24	M. W.	3	Trace	+++ 2.0 c.c.	1122100000	Neg.	5 yr.	C. S. L.; clinical symptoms
N. L.	1754	13	1 Dr. 5 S. E.	0.4	6.5649	0.0653	0.99	15.3	24	M. W.	0	Trace	+++ 2.0 c.c.	1122100000	Neg.	5 yr.	C. S. L.; clinical symptoms
N. L.	1796	14	1 Dr. 6 S. E.	0.4	6.8323	0.0729	1.06	1.07	24	M. W.	20	+++	+++ 1.5 c.c.	1122100000	+	5 yr.	C. S. L.
N. L.	1852	15	1 Dr. 7 S. E.	0.4	7.0604	0.0732	1.03	Trace	24	M. W.	20	+++	+++ 1.5 c.c.	1122100000	+	5 yr.	C. S. L.
W. M.	3	24	3 S. E.	0.4	5.47	0.0558	1.02	3.59	24	M. W.	3	Trace	++++ 2.0 c.c.	22332100000	++++	2 yr.	C. S. L.
W. M.	215	25	4 S. E.	0.4	7.3150	0.0748	1.02	26.7	24	M. W.	0	Neg.	Trace 2.0 c.c.		++++	2 yr.	C. S. L.
J. M.	834	1	1 S. E.	0.4	11.7723	0.1197	1.01	0	34	M. W.	3	+	+++ 0.4 c.c.	1233210000	+++	12 yr.	C. S. L.; clinically positive
J. M.	967	4	4 S. E.	0.3	11.6145	0.1180	1.01	7.4	34	M. W	3	+	+++ 0.4 c.c.	1233210000	+++	12 yr.	C. S. L.; clinically positive
J. M.	1077	8	8 S. E.	0.3	5.9211	0.1181	1.99	0	34	M. W.	2	Trace	++++ 0.6 c.c.	1233210000	++	12 yr.	C. S. L.; clinically positive
J. M.	1803	12	12 S. E.	0.4	15.1383	0.1563	1.02	3.83	34	M. W.	2	Trace	+++ 1.0 c.c.	1233210000	++	10 yr	C. S. L.; clinically positive
M. U.	2604	24	3 S. E.	0.4	13.2086	0.1344	1.01	0.744	23	M. W.	8	++++	++++ 0.4 c.c.	2333210000	Neg.	3 yr.	C. S. L.
M. U.	2514	23	2 S. E.	0.4	14.7719	0.1515	1.02	0.660	23	M. W.	4	+	++++ 0.8 c.c.	2333210000	Neg.	3 yr.	C. S. L.
M. U.	2889	25	4 S. E.	0.4	6.5098	0.0704	1.08	73.0	23	M. W.	2	Trace	++++ 2.0 c.c.	2333210000	Neg.	3 yr.	C. S. L.
L. V.	379	41	33 S. E.	0.4	15.3696	0.1607	1.04	0.31	35	M. W.	2	Trace	++++ 0.4 c.c.	1233321000	+	14 yr.	C. S. L.
M. W.	154	39	2 S. E.	0.4	4.1003	0.0443	1.08	5.6	40	M. W.	1	Neg.	++ 1.0 c.c.	1223100000	Neg.	12 yr.	C. S. L., asymptomatic
M. W.	236	40	3 S. E.	0.4	11.2230	0.1380	1.22	2.9	40	M. W.	3	Neg.	++ 1.0 c.c.	1223100000	Neg.	12 yr.	C. S. L.; asymptomatic
M. W.	256	41	4 S. E.	0.4	13.2699	0.1441	1.08	26.5	40	M. W.	2	Neg.	++ 1.0 c.c.	1223100000	Neg.	12 yr.	C. S. L.; asymptomatic
M. W.	365	42	5 S. E.	0.4	17.7024	0.1820	1.02	0.55	40	M. W.	4	Neg.	++++ 1.5 c.c.	1223100000	Neg.	12 yr.	C. S. L.; asymptomatic
M. W.	456	44	7 S. E.	0.4	14.0442	0.1422	1.01	0.35	40	M. W.	0	Neg.	++++ 1.5 c.c.	1223100000	Neg.	12 yr.	C. S. L.; asymptomatic
M. W.	488	45	8 S. E.	0.4	7.8895	0.0887	1.12	1.12	40	M. W.	2	Neg.	++++ 1.5 c.c.	1223100000	Neg.	12 yr.	C. S. L.; asymptomatic
M. W.	705	46	9 S. E.	0.4	14.6793	0.1671	1.07	5.9	40	M. W.	0	Neg.	++++ 1.5 c.c.	1223100000	Neg.	12 yr.	C. S. L.; asymptomatic
M. W.	906	49	14 S. E.	0.4	7.5950	0.0740	0.97	0	40	M. W.	0	Trace	++++ 2.0 c.c.	1223100000	Neg.	12 yr.	C. S. L.; asymptomatic
M. W.	969	50	15 S. E.	0.4	13.8602	0.1510	1.08	11.03	40	M. W.	2	Trace	++++ 2.0 c.c.	1223100000	Neg.	12 yr.	C. S. L.; asymptomatic
M. W.	1670	52	17 S. E.	0.4	8.1100	0.0766	0.94	Trace	40	M. W.	1	Neg.	Neg. 2.0 c.c.	0000000000	Neg.	12 yr.	C. S. L.; asymptomatic
M. W.	1758	53	18 S. E.	0.4	14.5085	0.1649	1.13	6.06	40	M. W.	3	Neg.	Neg. 2.0 c.c.	0000000000	Neg.	12 yr.	C. S. L.; asymptomatic
M. W.	2520	54	20 S. E.	0.4	5.5003	0.0528	0.95	3.78	40	M. W.	4	Trace	Neg. 2.0 c.c.	0000000000	Neg.	12 yr.	C. S. L.; asymptomatic
G. W.	173	1	1 S. E.	0.4	15.2740	0.1666	1.09	4.8	43	M. W.	8	++	++++ 0.6 c.c.	1233210000	++++	2 yr.	C. S. L.; asymptomatic
G. W.	283	3	3 S. E.	0.4	13.7704	0.1470	1.06	0.0581	43	M. W.	2	+	++++ 0.6 c.c.	1233210000	++++	2 yr.	C. S. L.; asymptomatic
G. W.	337	4	4 S. E.	0.4	7.6056	0.1077	1.40	Trace	43	M. W.	2	+	++++ 0.6 c.c.	1233210000	++++	2 yr.	C. S. L.; asymptomatic
G. W.	369	5	5 S. E.	0.4	7.3245	0.0794	1.08	Trace	43	M. W.	0	Neg.	++++ 0.4 c.c.	1233210000	++++	2 yr.	C. S. L.; asymptomatic
G. W.	403	6	6 S. E.	0.4	7.4733	0.0768	1.02	1.30	43	M. W.	0	Neg.	++++ 0.4 c.c.	1233210000	++++	2 yr.	C. S. L.; asymptomatic
G. W.	440	7	7 S. E.	0.4	8.0911	0.0915	1.13	7.68	43	M. W.	1	Neg.	++++ 0.6 c.c.	1233210000	++++	2 yr.	C. S. L.; asymptomatic
G. W.	773	10	10 S. E.	0.4	15.8730	0.1566	1.00	Trace	43	M. W.	1	Neg.	++++ 0.6 cc..	1233210000	++++	2 yr.	C. S. L.; asymptomatic
G. W.	837	12	12 S. E.	0.4	7.0937	0.0853	1.20	0	43	M. W.	2	Trace	++ 0.6 c.c.	1233210000	++++	2 yr.	C. S. L.; asymptomacit
G. W.	903	13	13 S. E.	0.4	14.1045	0.1470	1.04	0.67	43	M. W.	2	Neg.	++ 0.6 c.c.	1233210000	++++	2 yr.	C. S. L.; asymptomatic
G. W.	1378	14	14 S. E.	0.4	9.9933	0.1066	1.06	6.2	43	M. W.	1	++	++++ 0.6 c.c.	1233210000	++++	2 yr.	C. S. L.; asymptomatic
G. W.	1423	15	15 S. E.	0.4	7.9843	0.0796	0.99	1.2	43	M. W.	1	++	++++ 0. 6c.c.	1233210000	++++	2 yr.	C. S. L.; asymptomatic
G. W.	1671	16	16 S. E.	0.4	7.5623	0.0772	1.02	0	43	M. W.	0	+	++++ 0.6 c.c.	1233210000	++++	2 yr.	C. S. L.; asymptomatic
G. W.	1793	18	18 S. E.	0.4	8.7361	0.0966	1.10	Trace	43	M. W.	2	Trace	++++ 0.8 c.c.	1233210000	+++	2 yr.	C. S. L.; asymptomatic
G. W.	2363	21	19 S. E.	0.4	6.4300	0.0686	1.07	1.45	43	M. W.	1	Trace	++++ 0.8 c.c.	1233210000	++++	2 yr.	C. S. L.; asymptomatic

TABLE I—Cont'd
TERTIARY SYPHILIS—Cont'd
INTERVAL 48 HOURS—Cont'd

G. W.	2454	22	20 S. E.	0.4	7.8503	0.0845	1.07	7.10	43	M. W.	0	Trace	++++ 0.8 c.c.	1233210000	+++	2 yr.	C. S. L.; asymptomatic
G. W.	2519	23	21 S. E.	0.4	14.0075	0.1492	1.06	0.6702	43	M. W.	0	Trace	++++ 1.5 c.c.	1233210000	+++	2 yr.	C. S. L.; asymptomatic
G. W.	2715	24	22 S. E.	0.4	12.8588	0.1340	1.04	Trace	43	M. W.	2	Trace	++++ 1.5 c.c.	1233210000	+++	2 yr.	C. S. L.; asymptomatic
G. W.	2879	25	23 S. E.	0.4	11.9955	0.1328	1.10	4.51	43	M. W.	0	Trace	++++ 1.5 c.c.	1233210000	+++	2 yr.	C. S. L.; asymptomatic
W. Y. D.	339	11	2 S. E.	0.4	6.4510	0.0721	1.11	1.37	40	M. W.	2	Neg.	++++ 0.6 c.c.	2233221000	++++	16 yr.	C. S. L.; clinical symptoms
W. Y. D.	358	13	3 S. E.	0.4	6.7190	0.0711	1.05	3.51	40	M. W.	0	Trace	++++ 0.6 c.c.	2233221000	++++	16 yr.	C. S. L.; clinical symptoms
W. Y. D.	1767	21	11 S. E.	0.4	5.0984	0.0513	1.00	5.84	40	M. W.	0	Trace	++++ 0.6 c.c.	123321000	++++	16 yr.	C. S. L.; clinical symptoms
W. Y. D.	1801	22	12 S. E.	0.4	5.4808	0.0763	1.39	3.93	40	M. W.	3	Neg.	+++ 0.8 c.c.	1122100000	++++	16 yr.	C. S. L.; clinical symptoms
W. Y. D.	2322	23	13 S. E.	0.4	7.7742	0.0668	0.85	Trace	40	M. W.	0	Neg.	+++ 0.8 c.c.	1122100000	++++	16 yr.	C. S. L.; clinical symptoms
S. G.	1476	53	31 S. E.	0.4	6.3923	0.0719	1.12	2.78	36	M. W.	4	++	++++ 0.2 c.c.	5555442100	++++	4 yr.	G. P.; clinical symptoms
S. G.	2881	58	35 S. E.	0.4	8.3722	0.0965	1.15	8.28	36	M. W.	6	++	++++ 0.2 c.c.	5555442100	++++	4 yr.	G. P.; clinical symptoms
S. G.	3009	60	36 S. E.	0.4	4.9998	0.0554	1.10	7.22	36	M. W.	2	Trace	++++ 0.2 c.c.	5555442100	++++	4 yr.	G. P.; clinical symptoms
C. V.	151	40	2 S. E.	0.2	10.8939	0.1179	1.08	3.39	23	F. W.	15	Neg.	++++ 0.2 c.c.	5555431000	+++	?	G. P.; clinical manifestations. In institution
C. V.	367	43	5 S. E.	0.2	12.021	0.1267	1.05	Trace	23	F. W.	3	++++	++++ 0.2 c.c.	5555431000	+++	?	G. P.; clinical manifestations. In institution
C. V.	454	44	6 S. E.	0.2	13.1324	0.1403	1.06	0.35	23	F. W.	8	++++	++++ 0.2 c.c.	5555431000	+++	?	G. P.; clinical manifestations. In institution
W. C.	492	4	1 S. E.	0.4	15.5382	0.1874	1.20	4.4	42	M. W.	20	++++	++ 0.2 c.c.	5555431000	++++	23 yr.	G. P.
D. D.	444	10	1 S. E.	0.4	15.1354	0.1602	1.05	0	35	M. W.	13	++	++++ 0.2 c.c.	5555431000	++++	18 yr.	G. P.
H. H.	1473	72	50 S. E.	0.4	6.1384	0.0665	1.08	3.007		M. W.	22	++++	++++ 0.1 c.c.	5555554300	Neg.		G. P.; clinical manifestations
M. O.	73	17	9 S. E.	0.4	9.1313	0.1046	1.14	1.8	50	M. W.	4	++++	++++ 0.1 c.c.	5554432100	++++		G. P.
M. S.	5	21	13 S. E.	0.4	7.8727	0.0948	1.20	0.52	34	M. W.	6	++++	++++ 0.1 c.c.	5555421000	++++	11 yr.	G. P.; clinically +; died in institution.
S. I. L.	420	36	11 S. E.	0.4	14.6119	0.1581	1.08	Trace	27	M. W.	3	++	++ 0.2 c.c.	5555542100	+	10 yr.	G. P.; clinical manifestations
E. A.	116	36	6 S. E.	0.4	13.3308	0.1386	1.03	0.15	29	M. W.	5	+	++++ 0.2 c.c.	5554310000	++++	9 yr.	Meningo-vasculitis
E. A.	203	38	7 S. E.	0.4	7.3760	0.0791	1.07	8.8	29	M. W.	5	+	++++ 0.2 c.c.	5554310000	++++	9 yr.	Meningo-vasculitis
E. A.	237	39	8 S. E.	0.4	4.6688	0.0592	1.27	14.7	29	M. W.	10	++	++++ 0.2 c.c.	5554310000	++++	9 yr.	Meningo-vasculitis
E. A.	424	40	9 S. E.	0.4	7.0463	0.0701	0.99	1.43	29	M. W.	10	++	++++ 0.2 c.c.	5554310000	++++	9 yr.	Meningo-vasculitis
E. A.	484	41	10 S. E.	0.4	7.9663	0.0979	1.10	0	29	M. W.	8	++	++++ 0.2 c.c.	2332100000	++++	9 yr.	Meningo-vasculitis
E. A.	2882	51	14 S. E.	0.4	5.5459	0.0639	1.15	31.3	29	M. W.	6	++	++++ 0.2 c.c.	2332100000	Neg.	9 yr.	Meningo-vasculitis
W. I. L.	7	32	5 S. E.	0.4	6.7736	0.0721	1.06	0.93	32	M. W.	4	++	++++ 0.2 c.c.	5555431000	++++	4 yr.	Meningo-vasculitis
W. I. L.	216	33	6 S. E.	0.4	3.7809	0.0391	1.03	35.9	32	M. W.	4	++	++++ 0.2 c.c.	5555431000	++++	4 yr.	Meningo-vasculitis
McD.	383	20	15 S. E.	0.4	8.9395	0.0863	1.007	2.31	26	M. W.	3	++	++++ 0.4 c.c.	5433210000	++++	11 yr.	Optic atrophy
McD.	423	21	16 S. E.	0.4	7.1342	0.0721	1.01	1.38	26	M. W.	0	Neg.	++++ 1.5 c.c.	5433210000	++++	11 yr.	Optic atrophy
McD.	465	22	17 S. E.	0.4	7.8246	0.0790	1.009	3.80	26	M. W.	3	++	++++ 1.5 c.c.	5433210000	++++	11 yr.	Optic atrophy
McD.	485	23	18 S. E.	0.4	7.5556	0.0879	1.05	26.1	26	M. W.	2	Neg.	++++ 1.5 c.c.	5433210000	Neg.	11 yr.	Optic atrophy
P. A. T.	425	2	1 S. E.	0.4	6.9960	0.0715	1.02	0	46	M. W.	25	++++	++++ 0.4 c.c.	5555431000	++++	24 yr.	Optic atrophy
P. A. T.	462	3	2 S. E.	0.4	14.2899	0.1518	1.06	0.33	46	M. W.	20	++++	++++ 0.4 c.c.	5555431000	++++	24 yr.	Optic atrophy
P. A. T.	490	4	3 S. E.	0.4	13.2810	0.1530	1.13	Trace	46	M. W.	12	++++	++++ 0.4 c.c.	5555431000	++++	24 yr.	Optic atrophy
J. E.	2710	6	12 S. E.	0.4	13.1397	0.1133	0.86	0.882	44	M. W.	3	+	++++ 0.8 c.c.	123321000	++++		Tabes
J. K.	341	78	40 S. E.	0.4	6.8295	0.0780	1.14	5.13	31	M. W.	2	Neg.	++++ 1.0 c.c.	1123210000	+	7 yr.	Tabes; had been strongly positive
J. K.	356	79	41 S. E.	0.4	5.6208	0.0587	1.04	0	31	M. W.	0	Neg.	++++ 1.0 c.c.	1123210000	+	7 yr.	Tabes; had been strongly positive
J. K.	381	80	42 S. E.	0.4	15.2580	0.1656	1.08	Trace	31	M. W.	2	Neg.	++++ 1.0 c.c.	1123210000	+	7 yr.	Tabes; had been strongly positive
J. K.	422	81	43 S. E.	0.4	7.2164	0.0742	1.02	0	31	M. W.	1	Neg.	++++ 1.0 c.c.	1123210000	Neg.	7 yr.	Tabes; had been strongly positive
J. K.	466	82	44 S. E.	0.4	6.9384	0.0725	1.04	4.13	31	M. W.	3	Neg.	++++ 1.0 c.c.	1123210000	Neg.	7 yr.	Tabes; had been strongly positive
J. K.	853	84	46 S. E.	0.4	10.4782	0.1078	1.02	21.2	31	M. W.	0	Trace	++++ 1.0 c.c.	1123210000	Neg.	7 yr.	Tabes; had been strongly positive
J. K.	1027	85	47 S. E.	0.4	4.4465	0.0465	1.04	2.10	31	M. W.	2	Trace	+++ 1.0 c.c.	1123210000	Neg.	7 yr.	Tabes; had been strongly positive
J. K.	1094	86	48 S. E.	0.4	8.0650	0.0868	1.07	1.15	31	M. W.	0	Neg.	+++ 1.0 c.c.	1123210000	Neg.	7 yr.	Tabes; had been strongly positive
J. K.	1338	87	49 S. E.	0.4	14.6270	0.1586	1.08	4.41	31	M. W.	0	Neg.	+++ 1.0 c.c.	1123210000	Neg.	7 yr.	Tabes; had been strongly positive
J. K.	2364	96	50 S. E.	0.4	7.0800	0.0736	1.03	13.5	31	M. W.	3	++	++++ 0.6 c.c.	5555431000	++++	7 yr.	Tabes; fluid bcame stronger again with paretic curve.
J. K.	2885	97	51 S. E.	0.4	5.8013	0.0649	1.11	3.08	31	M. W.	5	++	++++ 0.6 c.c.	5555431000	++++	7 yr.	
W. T.	1886	6	1 S. E.	0.4	5.6978	0.0759	1.33	0	45	M. W.	24	Trace	++++ 0.4 c.c.	1233210000	++++	2 yr.	Tabes
M. T.	1848	19	11 S. E.	0.3	7.147	0.0729	1.02	3.43	51	F. W.	0	Neg.	Neg. 2.0 c.c.	0000000000	Neg.	30 yr.	Tabes; had been strongly +
M. T.	2566	24	16 S. E.	0.3	6.4076	0.0711	1.10	0.703	51	F. W.	2	Neg.	Neg. 2.0 c.c.	0000000000	Neg.	30 yr.	Tabes

TABLE I—Cont'd
TERTIARY SYPHILIS—Cont'd
INTERVAL 48 HOURS—Cont'd

PATIENT	SERIAL NO.	NO. PREVIOUS I. V. INJEC.	NO. PREVIOUS I. S. INJEC.	DOSE OF DRUG (SAL.)	WT. OF SPECIMEN		PER CENT SOLIDS	AS. IN MG. PER 100 GMS. DRIED SPEC.	AGE	SEX AND COLOR	SPINAL FLUID FINDINGS				BLOOD WASS.	DURATION OF INFECTION	DIAGNOSIS AND REMARKS
					MOIST	DRY					CELLS	GLOB.	WASSERMANN	GOLD SOL			
B. W.	2606	29	17 S. E.	0.4	13.9581	0.1476	1.06	5.08	39	M. W.	4	Neg.	Neg. 2.0 c.c.	1112321000	+++	12 yr.	Tabes
I. E.	836	26	15 S. E.	0.4	6.6488	0.0692	1.04	36.1	36	M. W.	2	+	++++ 0.8 c.c.	55555431000	Neg.	20 yr.	Tabes and optic atrophy
J. McN.	522	10	1 S. E.	0.4	13.5425	0.1452	1.07	2.45	34	M. W.	5	++	++++ 0.4 c.c.	1233210000	++++	11 yr.	Tabes
J. McN.	1375	20	1 Dr. 11 S. E.	0.4	13.5750	0.1420	1.05	0.704	34	M. W.	5	++	++++ 0.4 c.c.	1233210000	++++	11 yr.	Tabes
J. McN.	1471	21	1 Dr. 12 S. E.	0.4	15.5135	0.1613	1.03	3.71	34	M. W.	5	++	++++ 0.4 c.c.	1233210000	++++	11 yr.	Tabes and optic atrophy
M. A.	364	44	34 S. E.	0.4	13.2293	0.1513	1.14	0.66	49	M. W.	5	++	++++ 0.4 c.c.	5555554321	++++	2 yr.	Tabo-paresis
S. M.	327	27	10 S. E.	0.4	11.7402	0.1212	1.02	0.41	42	M. W.	8	++	++++ 0.6 c.c.	1122100000	++++	16 yr.	Tabes
O. S.	339	3	2 S. E.	0.4	6.4137	0.0857	1.33	7.0		M. W.	15	++++	++++ 0.2 c.c.	2233210000	+++		Tabes
S. I. N.	703	11	2 S. E.	0.4	14.6226	0.1575	1.07	0	33	M. W.	10	+++	++++ 0.6 c.c.	1233210000	++++	11 yr.	Tabes (mild)
W. O.	284	30	25 S. E.	0.4	12.8123	0.1368	1.06	0	55	M. W.	5	++	+++ 0.6 c.c.	1233210000	Neg.	32 yr.	Tabes (quiescent)
F. D.	854	13	1 S. E.	0.4	8.7270	0.0885	1.01	0.266	23	M. W.	40	++++	++++ 0.1 c.c.	1123210000	++++	3 yr.	C. S. L.; asymptomatic
INTERVAL 72 HOURS (15 CASES)																	
D. D.	1346	10	1 S. E.	0.4	6.0255	0.0609	1.01	9.8	39	M. W.	10	++	++++ 0.4 c.c.	1233210000	++++	8 yr.	C. S. L.; asymptomatic
D. D.	887	15	6 S. E.	0.4	7.5003	0.0877	1.16	0.57	39	M. W.	2	++	++++ 0. 8 c.c.	1233210000	++++	8 yr.	C. S. L.; asymptomatic
W. M.	486	26	5 S. E.	0.4	6.8206	0.0802	1.10	3.10	24	M. W.	2	Trace	Neg. 2.0 c.c.	0000000000	++++		C. S. L.; had been positive
M. U.	2455	22	2 S. E.	0.4	7.3864	0.0791	1.06	5.05	23	M. W.	4	++++	++++ 0.4 c.c.	2333210000	Neg.	3 yr.	C. S. L.; clinical symptoms
M. W.	1075	51	16 S. E.	0.4	7.5995	0.0806	1.06	1.24	40	M. W.	6	++	++++ 2.0 c.c.	1223100000	Neg.	12 yr.	C. S. L.; asymptomatic
C. O. S.	1883	18	1 S. E.	0.4	6.0527	0.0791	1.30	Trace	32	M. W.	8	++	++++ 0.2 c.c.	5555431000	++++		G. P.; clinical manifestations
S. I. L.	458	38	12 S. E.	0.4	15.5286	0.1722	1.108	0.29	27	M. W.	5	+	++ 0.2 c.c.	5555542100	+	10 yr.	G. P.; clinical symptoms
C. V.	179	40	2 S. E.	0.2	4.8270	0.0498	1.03	4.0	23	F. W.	3	Neg.	++++ 0.2 c.c.	5555431000	++++		G. P.; clinical symptoms
C. V.	207	41	3 S. E.	0.2	14.9960	0.1567	1.04	1.60	23	F. W.	3	++++	++++ 0.2 c.c.	5555431000	++++		G. P.; clinical symptoms
C. V.	315	42	4 S. E.	0.2	9.9721	0.1043	1.04	0.96	23	F. W.	2	++++	++++ 0.2 c.c.	5555431000	++++		G. P.; clinical symptoms
F. E.	342	14	2 S. E.	0.4	5.7827	0.0780	1.34	0	49	M. W.	3	+	++++ 0.4 c.c.	1223210000	++++	12 yr.	Tabes; clinically positive
F. E.	398	16	4 S. E.	0.4	15.5641	0.1715	1.10	11.6	49	M. W.	3	+	++++ 0.4 c.c.	1223210000	++++	12 yr.	Tabes; clinically positive
F. O. L.	1753	7	6 S. E.	0.4	5.6217	0.0536	0.95	3.73	45	M. W.	0	Trace	++++ 1.5 c.c.	1233210000	++++		Tabes
W. O.	163	28	22 S. E.	0.4	7.7110	0.0860	1.10	0	55	M. W.	3	++	+++ 0.4 c.c.	1233210000	Neg.	32 yr.	Tabes; clinically positive
W. O.	1756	34	28 S. E.	0.4	9.7190	0.0985	1.01	3.04	55	M. W.	2	++	+++ 0.4 c.c.	1233210000	Neg.	32 yr.	Tabes; clinically positive
INTERVAL 96 HOURS (3 CASES)																	
D. D.	2565	19	13 S. E.	0.4	5.6393	0.0642	1.13	4.67	39	M. W.	5	Trace	++++ 1.0 c.c.	1233210000	++++	8 yr.	C. S. L.; asymptomatic
C. B.	504	10	1 Dr. 1 S. E.	0.4	15.4315	0.1663	1.07	0.601	42	M. W.	10	++	++++ 0.2 c.c.	5555543100	++++	20 yr.	G. P. and optic atrophy. In institution
F. E.	438	17	5 S. E.	0.4	8.0365	0.0932	1.15	0	49	M. W.	4	++++	++++ 0.4 c.c.	1223210000	++++	12 yr.	Tabes; clinically positive

TABLE I—Cont'd
TERTIARY SYPHILIS—Cont'd
INTERVAL 120 HOURS (2 CASES)

D. D.	2457	19	12 S. E.	0.4	5.3805	0.0542	1.007	0	39	M. W.	6	Trace	++++ 1.0 c.c.	1233210000	++++	8 yr.	C. S. L.; asymptomatic
W. O.	1093	18	16 S. E.	0.4	21.9536	0.2353	1.07	Trace	55	M. W.	5	++	+++ 0.4 c.c.	1233210000	Neg.	32 yr.	Tabes; clinical manifestations

INTERVAL 2 WEEKS (2 CASES)

M. U.	2366	21	1 S. E.	0.4	1.5100	0.0096	0.63	0	23	M. W.	10	++++	++++ 0.4 c.c.	2333210000	Neg.	3 yr.	C. S. L.; clinically positive
O. S.	400	3	3 S. E.	0.3	12.6216	0.1348	1.06	3.09	63	M. W.	8	++++	++++ 0.2 c.c.	2233210000	++++	?	Tabes; active

INTERVAL 1 MONTH (1 CASE)

O. S.	447	2	2 S. E.	0.3	14.5110	0.1593	1.09	1.59	63	M. W.	20	++++	++++ 0.2 c.c.	2233210000	+++	?	Tabes; active

INTERVAL 2 MONTHS (1 CASE)

T. U. B.	325	2	1 S. E.	0.2	12.6460	0.1320	1.04	2.27	38	M. W.	10	+	++++ 0.6 c.c.	1233210000	++++	31 yr.	Tabes; optic atrophy. Could not take arsphenamine. Was treated with another patient's serum.

INTERVAL 4 MONTHS (2 CASES)

K. A.	40	19	12 S. E.	0.4	12.4859	0.1399	1.12	0.71	33	M. W.	10	++++	++++ 0.4 c.c.	5554321000	++++	?	G. P.; clinical symptoms
T. U. B.	368	2	3 S. E.	0.2	14.3702	0.1540	1.07	0.32	38	M. W.	6	+	++++ 0.6 c.c.	1233210000	++++	31 yr.	Tabes
T. U B.	399	2	3 S. E.	0.2	13.4006	0.1434	1.07	0.34	38	M. W.	6	+	++++ 0.6 c.c.	1233210000	++++	31 yr.	Tabes; optic atrophy Could not take arsphenamine. Was treated with another patient's serum. Serial numbers 368, 399 were from the same specimen. This was unknown to the chemist who examined them separately. The results are here given to show how closely they check up.

Table II

Detailed Analysis of Table I, Based on Time Intervals, Giving the Number of Cases in Each Group with Blood and Spinal Fluid Wassermann, Number of Previous Intravenous and Intraspinal Injections, and Dose of Drug, Together with the Highest Arsenic Value, the Lowest Arsenic Value and the Average Amount Found in Each Group

INTERVAL—2 HOURS

II NEUROSYPHILIS: 1 case; blood and spinal fluid negative; had been strongly positive.

Amount of arsenic: 11 mg. after 0.4 gm., 16 I.V.'s and 2 I.S.'s previously; female, white, aged 22; meningitis.

INTERVAL—24 HOURS

II NEUROSYPHILIS: 1 case; blood negative, spinal fluid positive.

Amount of arsenic: 4.7 mg. after 0.4 gm., 18 I.V.'s; 9 Drainages, and 4 I.S.'s previously; male, black, aged 28, C. S. L.

INTERVAL—48 HOURS

II NEUROSYPHILIS: 6 cases; 6 with negative blood; 5 with positive spinal fluid, 1 with negative spinal fluid.

No. previous injections: 17-27 I.V.'s; 3-10 I.S.'s.

Dose: 0.4 gm.

Smallest amount of arsenic: 0 after 21 I.V.'s and 5 I.S.'s; male, black, aged 28; C. S. L.

Largest amount of arsenic: 11.6 mg. after 27 I.V.'s and 6 I.S.'s, male, white, aged 25; C. S. L.

Average amount of arsenic in this group: 3.44 mg.

INTERVAL—72 HOURS

II NEUROSYPHILIS: 1 case; blood and spinal fluid positive.

Amount of arsenic: 4.98 mg. after 0.4 gm. and 29 I.V.'s and 7 I.S.'s previously; female, white, aged 25; C. S. L.

INTERVAL—30 MINUTES

III NEUROSYPHILIS: 2 cases; blood and spinal fluids positive.

Smaller amount of arsenic: 0 after 0.4 gm., 12 I.V.'s and 3 I.S.'s previously; male, white, aged 39; C. S. L.

Larger amount of arsenic: 4.1 mg. after 0.3 gm., 5 I.V.'s and 5 I.S.'s previously, male, white, aged 34.

Average amount of arsenic in this group: 2.05 mg.

N. B. These patients were treated with salvarsanized serum obtained the day before from another patient as there would not be time in 30 minutes to prepare an auto-serum.

INTERVAL—1 HOUR

III NEUROSYPHILIS: 2 cases, blood and spinal fluid Wassermann positive.

Smaller amount of arsenic: 0.76 mg. after 0.4 gm., 16 I.V.'s and 7 I.S.'s previously, male, white, aged 34, tabes.

TABLE II—Cont'd.

Larger amount of arsenic: 2.29 mg. after 0.4 gm., and 11 I.V.'s, 1 Drainage, and 2 I.S.'s previously; male, white, aged 42, paresis.

Average amount of arsenic in this group: 1.53 mg.

N. B. These patients were treated with salvarsanized serum obtained the day before from another patient as there would not be time in 60 minutes to prepare an auto-serum.

INTERVAL—2 HOURS

III NEUROSYPHILIS: 15 cases, blood and spinal fluids positive.

No. previous Injections: 5-31 I.V.'s; 1-14 I.S.'s.

Dose: 0.3 gm., 2 cases; 0.4 gm., 13 cases.

Smallest amount of arsenic; 0 after 0.4 gm. and 10 I.V.'s and 1 I.S. previously, male, white, aged 34, tabes.

Largest amount of arsenic: 18.9 mg. after 0.4 gm. 21 I.V.'s and 14 I.S.'s previously, male, white, aged 39. C. S. L.

Average amount of arsenic in this group: 4:14 mg.

N. B. These patients were treated with salvarsanized serum obtained the day before from another patient as there would not be time in 2 hours to prepare an auto-serum.

INTERVAL—3 HOURS

III NEUROSYPHILIS: 4 cases; 1 with negative blood; 3 with positive blood; 4 positive spinal fluid.

No. Previous Injections: 7-29 I.V.'s; 3-12 I.S.'s.

Dose: 0.4 gm.

Smallest amount of arsenic: Trace in 2 cases; 1 after 44 I.V.'s and 11 I.S.'s; male, white, aged 29, meningo-vascular-syphilis; the other, after 29 I.V.'s and 12 I.S.'s; male, white, aged 42, early tabes.

Largest amount of arsenic: 0.237 mg. after 22 I.V.'s and 3 I.S.'s; male, white, aged 32; paresis.

Average amount of arsenic for this group: 0.8 mg.

N.B. These patients were treated with salvarsanized serum obtained the day before from another patient as there would not be time in 3 hours to prepare an auto-serum.

INTERVAL—4 HOURS

III NEUROSYPHILIS: 2 cases; blood and spinal fluids positive.

Smaller amount of arsenic: 3:30 mg. after 0.4 gm., 6 I.V.'s and 4 I.S.'s; male, white, aged 42; paresis.

Larger amount of arsenic: 58.5 mg. after 0.4 gm., 6 I.V.'s and 4 I.S.'s; white, aged 46; complete optic atrophy.

Average amount of arsenic in this group: 30.9 mg.

N. B. These patients were treated with salvarsanized serum obtained the day before from another patient as there would not be time in 4 hours to prepare an auto-serum.

TABLE II—Cont'd.

INTERVAL—24 HOURS

III NEUROSYPHILIS: 84 cases; 49 with negative blood Wassermann, 35 with positive blood Wassermann.

12 with negative spinal fluids.

4 with a positive spinal fluid Wassermann in amounts varying from 1.5-2.0 c.c.

33 with a positive spinal fluid Wassermann in amounts varying from 0.6-1 c.c.

35 with a positive spinal fluid Wassermann in amounts varying from 0.1-0.4 c.c.

No. Previous Injections: 2-66 I.V.'s; 1-41 I.S.'s

Dose: 0.2 gm., 1 case; 0.3 gm. 10 cases; 17 gm. 66 cases.

Smallest amount of arsenic: 0 arsenic in 9 cases.

Diagnoses in these cases were as follows: C.S.L., 3 cases; Optic atrophy, 1 case; Tabes, 5 cases.

Largest amount of arsenic: 38.3 mg. after 0.4 gm., 27 I.V.'s and 9 I.S.'s previously; male, white, aged 39; cured C.S.L. This patient's fluid at time of examination was negative, but it had been strongly positive 1 year after infection.

Average amount of arsenic in this group: 5.45 mg.

INTERVAL—48 HOURS

III NEUROSYPHILIS: 112 cases; 35 with negative blood; 6 with weakly positive blood; and 71 with strongly positive Wassermann.

7 with negative spinal fluids

22 with a positive spinal fluid Wassermann in amounts varying from 1.5-2.0 c.c.

46 with a positive spinal fluid Wassermann in amounts varying from 0.6-1 c.c.

37 with a positive spinal fluid Wassermann in amounts varying from 0.1-0.4 c.c.

No. Previous Injections: 1-96 I.V.'s; 1-50 I.S.'s.

Dose: 0.2 gm., 3 cases; 0.3 gm. 10 cases; 0.4 gm. 99 cases.

Smallest amount of arsenic: 0 arsenic in 14 cases; Diagnoses in these cases were as follows: C.S.L., 9 cases; Optic Atrophy, 1 case; Tabes, 3 cases; Paresis 1 case.

Largest amount of arsenic: 73.0 mg. after 0.4 gm., and 25 I. V.'s and 4 I.S.'s previously; male, white, aged 23; clinical diagnosis, C.S.L.; spinal fluid Wassermann rapidly becoming negative.

Average amount of arsenic in this group, 5.31 mg.

INTERVAL—72 HOURS

III NEUROSYPHILIS: 4 with negative blood Wassermann, 1 with weakly positive blood and 10 strongly positive blood Wassermann.

1 with negative spinal fluid

Table II—Cont'd.

2 with a positive spinal fluid Wassermann in amounts varying from 1.5-2.0 c.c.

1 with a positive spinal fluid Wassermann in amounts varying from 0.6-1.0 c.c.

11 with a positive spinal fluid Wassermann in amounts varying from 0.2-0.4 c.c.

No. Previous Injections: 7-51 I.V.'s; 1-28 I.V.'s.

Dose: 0.2 gm., 3 cases; 0.4 gm. 12 cases.

Smallest amount of arsenic: 0 arsenic in 2 cases; one had had 0.4 gm. and 14 I.V.'s and 2 I.S.'s; strongly positive spinal fluid and blood Wassermann; male, white, aged 49; tabes; the other had had 0.4 gm., 28 I.V.'s, 22 I.S.'s, strongly positive spinal fluid and negative blood Wassermann; male, white, aged 55, tabes.

Largest amount of arsenic: 11.6 mg. after 0.4 gm., and 16 I.V.'s and 4 I.S.'s; male, white, aged 49, tabetic. (The same patient is cited above with 0 arsenic)

Average amount of arsenic in this group: 2.99 mg.

INTERVAL—96 HOURS

III NEUROSYPHILIS: 3 cases; blood positive in all.

1 with a positive spinal fluid Wassermann with 1 c.c.

2 with a positive spinal fluid Wassermann with amounts varying from 0.2 to 0.4 c.c.

No. previous injections: 10-19 I. V.'s; 1-13 I. S.'s.

Dose 0.4 gm.

Smallest amount of arsenic: 0 after 17 I. V.'s and 5 I. S.'s; strongly positive spinal fluid; male, white, aged 41; tabes.

Largest amount of arsenic: 4.67 mg. after 19 I. V.'s and 13 I. S.'s; fluid gradually becoming negative; male, white, aged 39; C. S. L.

Average amount of arsenic in this group: 1.757 mg.

INTERVAL—120 HOURS

III NEUROSYPHILIS: 2 cases; 1 with negative blood; 1 with positive blood; spinal fluid positive in both.

Smaller amount of arsenic: 0 after 0.4 gm. and 19 I. V.'s and 12 I. S.'s; male, white, aged 39; C. S. L.

Larger amount of arsenic: trace after 0.4 gm. and 18 I. V.'s and 16 I. S.'s; male, white, aged 55; tabes.

Average amount of arsenic: 0.

INTERVAL—2 WEEKS

III NEUROSYPHILIS: 2 cases; 1 with negative blood; 1 with positive blood; spinal fluid strongly positive in both.

Smaller amount of arsenic: 0 after 0.4 gm., and 21 I.V.'s and 1 I.S.; male, white, aged 23; C. S. L.

TABLE II—Cont'd.

Larger amount of arsenic: 3.09 mg. after 0.3 gm., and 3 I. V.'s and 3 I.S.'s; male, white, aged 63; tabes.
Average amount of arsenic; 1.54 mg.

INTERVAL—1 MONTH

III NEUROSYPHILIS: 1 case; strongly positive blood and spinal fluid.
Amount of arsenic: 1.59 mg. after 0.3 gm. and 2 I. V.'s and 2 I. S.'s; white, aged 63; tabes.

INTERVAL—2 MONTHS

III NEUROSYPHILIS: 1 case; positive blood and spinal fluid.
Amount of arsenic: 2.27 mg. after 0.2 gm. and 2 I.V.'s and 1 I.S.; male, white, aged 38; Tabes with Optic Atrophy.

INTERVAL—4 MONTHS

III NEUROSYPHILIS: 2 cases; blood and spinal fluid, strongly positive.
Smaller amount of arsenic: 0.32 mg. after 2 I. V.'s received 4 months previously, and 3 I. S.'s in the meantime. The patient reacted so severely to intravenous injections, that he was treated intraspinally with salvarsanized serum from another patient; male, white, aged 38; tabes with optic atrophy.
Larger amount of arsenic: 0.71 mg. after 0.4 gm. and 19 I. V.'s and 12 I. S.'s; male, white, aged 33; paresis.
Average amount of arsenic: 0.52 mg.

TABLE III

A CLASSIFICATION BASED ON CLINICAL DIAGNOSIS AND QUANTITY OF ARSENIC PRESENT IN THE CEREBRO-SPINAL FLUID

	NO ARSENIC	
Tabes	Serial No. 491	2 Hr.
	459	24 “
	1030	“ “
	1668	“ “
	520	“ “
	212	“ “
	1488	“ “
	703	48 “
	1886	“ “
	284	“ “
	356	“ “
	422	72 “
	342	“ “
	163	
	438	96 “
Optic Atrophy	1760	24 “
	425	48 “

Table III—Cont'd.

NO ARSENIC

Paresis		444	48 “
C. S. L.		1526	30 Minutes
		654	24 Hr.
		538	
		328	48 “
		1755	
		834	“ “
		1077	“ “
		906	“ “
		837	“ “
		1671	“ “
		484	“ “
		2457	120 Hr.
		2366	3 Weeks

TRACE ARSENIC

Tabes	Serial No.	464	24 Hr.
		767	“ “
		583	“ “
		655	“ “
		1076	“ “
		381	48 “
		1093	120 “
Optic Atrophy		490	48 “
Paresis		420	48 “
		367	72 “
		1883	2 “
C. S. L.		954	3 “
		652	“ “
		582	24 “
		2711	“ “
		517	“ “
		419	“ “
		357	48 “
		428	“ “
		1379	“ “
		1852	“ “
		1670	“ “
		2322	“ “
		337	“ “
		369	“ “
		773	“ “
		1793	“ “

0.29 MG. TO 5 MG. OF ARSENIC PER 100 GM. DRIED SPEC.

Tabes	Serial No.	970	1 Hr.	0.76 mg.
		1586	24 “	2.62 “
		171	“ “	1.08 “
		382	“ “	1.37 “
		427	“ “	1.26 “

Table III—Cont'd.

0.29 mg. to 5.0 mg. of Arsenic per 100 gm. dried spec. (continued)

	9	" "	4.73 "
	174	" "	1.90 "
	402	" "	2.0 "
	510	" "	4.0 "
	657	" "	4.30 "
	769	" "	2.20 "
	890	" "	4.70 "
	2518	" "	0.84 "
	340	" "	3.66 "
	2885	48 "	3.08 "
	466	" "	4.13 "
	1027	" "	2.10 "
	1094	" "	1.15 "
	1338	" "	4.41 "
	2710	" "	0.882 "
	1848	" "	3.43 "
	2566	" "	0.703 "
	522	" "	2.45 "
	1375	" "	0.74 "
	1471	" "	3.71 "
	1753	72 "	3.73 "
	1756	" "	3.04 "
	400	2 Wks.	3.09 "
	447	1 Mo.	1.59 "
	325	2 "	2.27 "
	368	4 "	0.32 "
	399	" "	0.34 "
Optic Atrophy	1513	2 Hr.	1.76 "
	584	3 "	0.846 "
	1376	24 "	3.09 "
	505	" "	2.16 "
	383	48 "	2.31 "
	465	2 "	3.80 "
	423	" "	1.38 "
	462	" "	0.33 "
	325	2 Mos.	2.27 "
Paresis	508	1 Hr.	2.29 "
	600	2 "	0.61 "
	507	2 "	0.575 "
	463	" "	0.32 "
	2349	3 "	2.37 "
	578	4 "	3.30 "
	48	24 "	0.66 "
	158	" "	4.05 "
	722	" "	0.467 "
	361	" "	0.54 "
	503	" "	2.188 "
	519	" "	4.14 "
	454	48 "	0.35 "

TABLE III—Cont'd.

0.29 MG. TO 5.0 MG. OF ARSENIC PER 100 GM. DRIED SPEC. (continued)

Paresis	Serial No. 492	48 Hr.	4.40 "
	1476	" "	2.78 "
	1473	" "	3.007 "
	73	" "	1.18 "
	5	" "	0.52 "
	1151	" "	3.39 "
	364	" "	0.66 "
	458	72 "	0.29 "
	207	" "	1.60 "
	315	" "	0.96 "
	179	" "	4.0 "
	504	96 "	0.601 "
	40	4 Mos.	0.71 "
C. S. L.	987	30 Minutes	4.1 "
	1884	2 Hr.	2.48 "
	329	" "	1.06 "
	509	" "	5.0 "
	1002	" "	1.32 "
	254	24 "	4.7 "
	401	" "	0.65 "
	426	" "	1.3 "
	346	" "	0.79 "
	363	" "	2.9 "
	405	" "	3.40 "
	700	" "	1.83 "
	702	" "	2.04 "
	117	" "	2.64 "
	461	" "	4.30 "
	889	" "	3.05 "
	1170	" "	2.9 "
	1093	" "	4.44 "
	282	" "	4.19 "
	1229	" "	1.21 "
	442	" "	1.05 "
	516	" "	4.04 "
	701	" "	1.34 "
	521	" "	2.20 "
	366	48 "	1.5 "
	455	" "	0.64 "
	2323	" "	1.44 "
	1796	" "	1.07 "
	1803	" "	3.83 "
	2604	" "	0.744 "
	2514	" "	0.66 "
	2520	" "	3.78 "
	1801	" "	3.93 "
	905	" "	4.50 "
	952	" "	2.8 "
	854	" "	0.266 "
	384	" "	3.50 "
	1424	" "	4.8 "
	1527	" "	2.82 "
	1673	" "	2.36 "
	3	" "	3.59 "

TABLE III—Cont'd.

0.29 MG. TO 5.0 MG. OF ARSENIC PER 100 GM. DRIED SPEC. (continued)

C. S. L.	Serial No.	379	" "	0.31 "
		236	" "	2.9 "
		365	" "	0.55 "
		456	" "	0.35 "
		488	" "	1.12 "
		339	" "	1.37 "
		358	" "	3.51 "
		7	" "	0.93 "
		116	" "	0.15 "
		424	" "	1.43 "
		1761	72 "	4.98 "
		1887	" "	0.57 "
		486	" "	3.10 "
		1075	" "	1.24 "
		2565	96 "	4.67 "

5 TO 20 MG. OF ARSENIC PER 100 GM. DRIED SPEC.

Tabes	Serial No.	170	24 Hr.	12.5 mg.
		1851	" "	6.20 "
		518	" "	6.03 "
		1074	" "	5.8 "
		244	" "	16.6 "
		1342	" "	7.4 "
		1469	" "	7.13 "
		909	" "	12.3 "
		443	" "	10.8 "
		953	" "	8.87 "
		212	" "	5.6 "
		2606	48 "	5.08 "
		339	" "	7.0 "
		440	" "	7.68 "
Paresis		833	2 Hr.	6.27 "
		506	24 "	19.6 "
		2881	48 "	8.28 "
		3009	" "	7.22 "
		203	" "	8.8 "
		237	" "	14.7 "
C. S. L.		437	2 Hr.	11.0 "
		2878	" "	18.9 "
		235	" "	9.09 "
		257	" "	13.1 "
		245	24 "	17.2 "
		1230	" "	12.0 "
		172	" "	8.47 "
		331	" "	6.9 "
		8	" "	8.0 "
		64	" "	20.0 "
		115	" "	7.90 "
		441	" "	11.4 "
		910	" "	18.3 "
		157	" "	11.7 "

TABLE III—Cont'd.

5 MG. TO 20 MG. OF ARSENIC PER 100 GM. DRIED SPEC.			
C. S. L.	Serial No. 39	48 "	6.9 "
	176	" "	11.6 "
	2883	" "	5.47 "
	2364	" "	13.5 "
	341	" "	5.13 "
	1754	" "	15.3 "
	967	" "	7.4 "
	154	" "	5.6 "
	705	" "	5.9 "
	969	" "	11.03 "
	1758	" "	6.06 "
	1767	" "	5.84 "
	2454	" "	7.10 "
	1378	" "	6.2 "
	2455	72 "	5.05 "
	1346	" "	9.8 "
	398	" "	11.6 "
20 MG. TO 50 MG. OF ARSENIC PER 100 GM. DRIED SPEC.			
Tabes	836	48 Hr.	36.1 mg.
Optic Atrophy	485	" "	26.1 "
Paresis	2882	" "	31.3 "
C. S. L.	164	24 "	34.9 "
	205	" "	23.9 "
	467	" "	38.3 "
	3014	48 "	40.5 "
	853	" "	21.2 "
	215	" "	26.7 "
	256	" "	26.5 "
	216	" "	35.9 "
50 MG. TO 73.0 MG. OF ARSENIC PER 100 GM. DRIED SPEC.			
Optic Atrophy	580	4 Hr.	58.5 mg.
C. S. L.	2889	48 "	73.0 "

SUMMARY

1. This article deals with the arsenic content of the cerebrospinal fluid of patients with neurosyphilis who were treated with combined intravenous and intraspinal injections according to the Swift-Ellis method. The drug used was salvarsan.

2. Sixty-three patients were investigated and 257 spinal fluids examined. The clinical diagnoses were as follows: cerebrospinal syphilis, 25 cases; tabes dorsalis, 19 cases (2 with optic atrophy); paresis, 15 cases (1 with optic atrophy); and simple optic atrophy, 4 cases.

3. The serological and clinical findings at the time these chemical examinations were made are recorded in Table I.

4. The specimens of spinal fluid, as shown by consulting Table I, were taken at intervals varying from 30 minutes to 4 months.

5. The size of the specimen, percentage solids, and the amount of arsenic in milligrams per 100 grams of dry specimen are contained under their respective headings in Table I.

6. Table II is a resume of the spinal fluid findings based on time intervals. The number of cases in each group, the blood and spinal fluid Wassermann, number of previous intravenous and intraspinal injections and dose of drug are given with the resulting highest arsenic value, lowest arsenic value and the average quantity found in each group.

7. In Table III the data are tabulated according to the quantity of arsenic demonstrated and the clinical classification of the patient. Six groups are arranged as follows: Group 1 showing no arsenic; Group 2 yielding a trace; Group 3 having from 0.29 to 5 milligrams per 100 grams of dried specimen; Group 4 containing 5 to 20 milligrams; Group 5 from 20 to 50 milligrams, and Group 6 from 50 to 73 milligrams metallic arsenic per 100 grams of dried specimen.

8. Of the 257 cerebrospinal fluids analyzed 12 per cent showed no arsenic at some period during treatment. Classified according to the clinical diagnosis, they fall into the following groups: tabes 6 per cent; optic atrophy 0.8 per cent; paresis 0.4 per cent; cerebrospinal syphilis 5.1 per cent.

Ten and one-half per cent of the fluids showed a trace of metallic arsenic at some examination: tabes 2.7 per cent; optic atrophy 0.4 per cent; paresis 1.1 per cent; cerebrospinal syphilis 6.2 per cent.

Forty-eight per cent of the spinal fluids contained from 0.29 to 5 mg. per 100 gm. of dried specimen; tabes 12 per cent; optic atrophy 3.5 per cent; paresis 10.1 per cent; cerebrospinal syphilis 21.8 per cent.

Twenty per cent of the spinal fluids showed 5 to 20 mg. per 100 gm. dried specimen; tabes 5.5 per cent; paresis 2.3 per cent; cerebrospinal syphilis 12 per cent.

Four and three-tenths per cent of the spinal fluids yielded 20 to 50 mg. per 100 gm. dried specimen; tabes 0.4 per cent; optic atrophy 0.4 per cent; general paresis 0.4 per cent; cerebrospinal syphilis 3.1 per cent.

Eight-tenths per cent of the spinal fluids showed from 50 to 73 mg. per 100 gm. dried specimen; optic atrophy 0.4 per cent; cerebrospinal syphilis 0.4 per cent.

9. Reference to the remarks under individual histories will reveal the fact that in some instances frequency of combined treatment was not uniform. Under these circumstances variations in the arsenic content of the spinal fluid should be expected.

10. A clinical discussion and interpretation of this paper will appear at the end of this series.

QUANTITATIVE STUDIES IN SYPHILIS FROM A CLINICAL AND BIOLOGICAL POINT OF VIEW

VII. Arsenic Content of the Spinal Fluid after Salvarsan and Drainage

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DURING our investigations on the arsenic content of the cerebrospinal fluid of patients treated by the Swift-Ellis method, a certain number of cases were selected for drainage for purposes of comparison. As the clinical material available at that time was not very abundant a number of patients who had had previous intraspinal treatments, as indicated in Table I, were taken for these observations.

Our studies were made on 40 patients and 72 cerebrospinal fluids. Of these 9 had secondary or tertiary syphilis but no symptoms referable to the central nervous system and were negative serologically in the fluid; 14 cases had cerebrospinal syphilis; 8 had tabes (1 with optic atrophy); 8 had paresis (1 with optic atrophy), and one case had simple optic atrophy.

Salvarsan was the drug employed for these analyses, prepared according to the method given in article IV. At the various intervals shown in Table I, 20-40 c.c. of spinal fluid were withdrawn.

Three histories of patients who had repeated drainages are presented to illustrate the variations in the quantity of arsenic which are met with in these examinations. (Reference should be made to articles I and V for a discussion of the method of calculation.)

Paresis: W. C.; male; aged 42; chancre in 1898. When first seen was very dull mentally and no history could be elicited.

Physical examination: Pupils unequal and irregular; right fixed to light, left sluggish; upper deep reflexes active and unequal on two sides; patellar jerks weak; Achilles absent; very slow mentally; speech slurring; tremors; memory very poor; habits untidy.

Serology:			
	Blood	6/ 6/21	++++
		6/14/22	++++
	Spinal Fluid	6/ 6/21	Cells 48 Glob. ++++ Wass. ++++ to 0.2 c.c. Gold Sol: 5555543100
		6/14/22	Cells 8 Glob. ++++ Wass. ++++ to 0.2 c.c. Gold Sol: 5555431000

Results: Patient showed no clinical improvement, gradually deteriorated and was committed to an institution.

Treatment and Arsenic Determinations:

PREVIOUS NO. I. V. INJECTIONS	PREVIOUS NO. I. S. INJECTIONS AND DRAINAGES	DOSE	INTERVAL AFTER I. V.	AS PER 100 GM. DRIED SPEC.
9	4 S.E. 3 Dr.	0.4 gm.	2 hours	0
10	4 S.E. 4 Dr.	0.4 "	2 "	0
11	4 S.E. 5 Dr.	0.4 "	1 hour	1.50 mg.
12	4 S.E. 6 Dr.	0.4 "	2 hours	9.3 "
14	4 S.E. 8 Dr.	0.4 "	2 "	1.41 "
15	4 S.E. 9 Dr.	0.4 "	2 "	3.15 "
16	4 S.E. 10 Dr.	0.4 "	2 "	3.15 "
17	4 S.E. 11 Dr.	0.4 "	2 "	0.735 "

Remarks: Where the first zero appears the interval between intravenous injections was 3½ months, the second one two weeks; the succeeding injections were also two weeks apart.

PARESIS: C. B.; male; age 42; history of penile chancre 17 years ago. For several years had had pains in extremities and failing vision. Wife stated husband had been very quarrelsome during past year and had shown gross memory and speech defects.

Physical examination: Pupils contracted, irregular and fixed to light; partial optic atrophy both eyes; deep reflexes of arms very weak; of legs abolished. Marked speech disturbance; memory very poor; noisy, aggressive and filthy in his habits.

Serology:	Blood	4/26/21	++++
		10/11/22	++++
	Spinal Fluid	4/26/21	Cells 10
			Glob. ++++
			Wass. ++++ to 0.2 c.c.
			Gold Sol: 5555543100
		10/11/22	Cells 8
			Glob. ++++
			Wass. ++++ to 0.2 c.c.
			Gold Sol: 5555543100

Results: Patient was an advanced paretic. He did not improve materially under treatment, but failed slowly and was finally sent to an institution where he died shortly afterwards.

Treatment and Arsenic Determinations:

PREVIOUS NO. I. V. INJECTIONS	PREVIOUS NO. I. S. INJECTIONS AND DRAINAGES	DOSE	INTERVAL AFTER I. V.	AS PER 100 GM. DRIED SPEC.
9	1 Dr.	0.4 gm.	48 hours	1.20 mg.
15	5 S.E. 2 Dr.	0.4 "	48 "	0.61 "
16	5 S.E. 3 Dr.	0.4 "	48 "	1.33 "
17	5 S.E. 4 Dr.	0.4 "	2 "	9.50 "
18	5 S.E. 5 Dr.	0.4 "	48 "	44.4 "
19	5 S.E. 6 Dr.	0.4 "	2 "	0 "
20	5 S.E. 7 Dr.	0.4 "	24 "	26.3 "
21	5 S.E. 8 Dr.	0.4 "	2 "	trace
22	5 S.E. 9 Dr.	0.4 "	2 "	0 "
24	5 S.E. 11 Dr.	0.4 "	3 "	trace

Remarks: The average intervals between intravenous injections were a month.

Paresis: J. F.; male; age 40; chancre 24 years ago; secondaries denied For one year had had epileptiform attacks. Complained of loss of memory, and inability to work as well as formerly.

Physical examination: Pupils unequal, irregular and fixed to light; all deep reflexes hyperactive and unequal on the two sides; mental stigmata of general paresis.

Serology:	Blood	12/26/18	++++
		8/12/22	++++
	Spinal Fluid	12/26/18	Cells 16 Glob. ++ Wass. ++++ to 0.2 c.c. Gold Sol: 5555532100
		8/12/22	Cells 10 Glob. ++++ Wass. ++++ to 0.2 c.c. Gold Sol: 5555532100

Results: Several remissions were induced but relapses occurred with slow progression of the disease. Patient still remains at home.

Treatment and Arsenic Determinations:

PREVIOUS NO. I. V. INJECTIONS	PREVIOUS NO. I. S. INJECTIONS AND DRAINAGES	DOSE	INTERVAL AFTER I. V.	AS PER 100 GM. DRIED SPEC.
51	9 S.E. 1 Dr.	0.4 gm.	4 hours	3.86 mg.
52	9 S.E. 2 Dr.	0.4 "	2 "	0.57 "
53	9 S.E. 3 Dr.	0.4 "	4 months	0.65 "
54	9 S.E. 4 Dr.	0.4 "	2 hours	0.59 "
55	9 S.E. 5 Dr.	0.4 "	4 "	0 "
56	9 S.E. 6 Dr.	0.4 "	3 "	6.70 "
57	9 S.E. 7 Dr.	0.4 "	72 "	27.8 '
58	9 S.E. 8 Dr.	0.4 "	2 "	2.04 "

Remarks: The intervals between the above intravenous treatments were approximately two weeks excepting the four months one indicated above when spinal fluid was taken before the injection of the salvarsan.

EXPLANATION OF ABBREVIATIONS USED IN TABLES:

I. V. = Intravenous injection
I. S. = Intraspinal injection
Dr. = Drainage
S. E. = Swift-Ellis method of intraspinal treatment
S. F. = Spinal Fluid
S.; Sal.; Salv. = Salvarsan
S. S. = Silver Salvarsan
Neo. = Neosalvarsan
Glob. = Globulin
Wass. = Wassermann
I = Primary Syphilis
II = Secondary Syphilis
III = Tertiary Syphilis
C. S. L. = Cerebro-spinal syphilis
G. P. = General paresis

(*Continued on page* 518.)

TABLE I

ARSENIC CONTENT OF THE SPINAL FLUID AFTER SALVARSAN AND DRAINAGE

PATIENT	SERIAL NO.	NO. PREVIOUS I. V. INJEC.	NO. PREVIOUS I. S. AND DRAINAGES	DOSE OF DRUG (SAL.)	WT. OF SPECIMEN		PER CENT SOLIDS	AS. IN MG. PER 100 GMS. DRIED SPEC.	AGE	SEX AND COLOR	SPINAL FLUID FINDINGS				BLOOD WASS.	DURATION OF INFECTION	DIAGNOSIS AND REMARKS
					MOIST	DRY					CELLS	GLOB.	WASSERMANN	GOLD SOL			
SECONDARY SYPHILIS INTERVAL—1½ HOURS																	
McC.	986	10	0	0.4	4.8673	0.0477	0.98	5.5	35	M. W.	Neg.	Neg.	Neg. 2.0 c.c.	0000000000	++++	4 mos.	No neurosyphilis. Drainage for examination.
INTERVAL—24 HOURS																	
J. O. H.	989	8	0	0.4	6.7145	0.0638	0.95	Trace	18	M. W.	Neg.	Neg.	Neg. 2.0 c.c.	0000000000	Neg.	15 mos.	No neurosyphilis; for examination only. 3 daily injections 0.3 gm. preceding drainage.
INTERVAL—48 HOURS																	
B. O. M.	1850	14	0	0.4	2.9295	0.0328	1.12	15.2	27	M. W.	Neg.	Neg.	Neg. 2.0 c.c.	0000000000	Neg.	5 mos.	No neurosyphilis. Drainage for fluid examination.
J. A. C.	1265	2	0	0.4	6.0940	0.0690	1.13	Trace	25	M. W.	Neg.	Neg.	Neg. 2.0 c.c.	0000000000	++++	1 yr.	No neurosyphilis. Drainage for fluid examination.
INTERVAL—96 HOURS																	
P. A.	2365	9	0	0.3	4.3250	0.0450	1.04	7.40	29	M. W.	Neg.	Neg.	Neg. 2.0 c.c.	0000000000	+++	1 yr.	No neurosyphilis. Drainage for fluid examination.
TERTIARY LUES INTERVAL—1 HOUR																	
W. C.	1096	11	4 S. E. 5 Dr.	0.4	12.7402	0.1405	1.105	1.50	42	M. W.	10	++++	++++ 0.2 c.c.	5555431000	++++	23 yr.	Paresis. Sent to institution.

TABLE I—Continued

TERTIARY LUES—Continued

INTERVAL—2 HOURS

C. B.	1169	17	5 S. E. 4 Dr.	0.4	13.7949	0.1580	1.15	9.50	42	M. W.	10	++	++++ 0.2 c.c.	5555543100	++++	20 yr.	Optic atrophy; Paresis. Sent to institution.
C. B.	1528	19	5 S. E. 6 Dr.	0.4	6.9066	0.0787	1.13	0	42	M. W.	20	++++	++++ 1.0 c.c.	5555543100	++++	20 yr.	Optic atrophy; Paresis. Sent to institution.
C. B.	1882	21	5 S. E. 8 Dr.	0.4	11.4112	0.1312	1.14	Trace	42	M. W.	10	++++	++++ 0.2 c.c.	5555543100	++++	20 yr.	Optic atrophy; Paresis. Sent to institutioon.
C. B.	1998	22	5 S. E. 9 Dr.	0.4	15.7838	0.1993	1.26	0	42	M. W.	18	++++	++++ 0.2 c.c.	5555543100	++++	20 yr.	Optic atrophy; Paresis. Sent to institution.
W. C.	1004	9	4 S. E. 3 Dr.	0.4	5.3437	0.0552	1.03	0	42	M. W.	8	++++	++++ 0.2 c.c.	5555543100	++++	23 yr.	Paresis. Sent to institution.
W. C.	1081	10	4 S. E. 4 Dr.	0.4	5.3881	0.0588	1.09	0	42	M. W.	6	++++	++++ 0.2 c.c.	5555543100	++++	23 yr.	Paresis. Sent to institution.
W. C.	1267	12	4 S. E. 6 Dr.	0.4	6.5150	0.0750	1.15	9.3	42	M. W.	5	++++	++++ 0.2 c.c.	5555431000	++++	23 yr.	Paresis. Sent to institution.
W. C.	1666	14	4 S. E. 8 Dr.	0.4	13.5999	0.1411	1.03	1.41	42	M. W.	10	++++	++++ 0.2 c.c.	5555431000	++++	23 yr.	Paresis. Sent to institution.
W. C.	1768	15	4 S. E. 9 Dr.	0.4	5.4604	0.0631	1.15	3.15	42	M. W.	7	++++	++++ 0.2 c.c.	5555431000	++++	23 yr.	Paresis. Sent to institution.
W. C.	1847	16	4 S. E. 10 Dr.	0.4		0.0462		3.59	42	M. W.	12	++++	++++ 0.2 c.c.	5555431000	++++	23 yr.	Paresis. Sent to institution.
W. C.	1881	17	4 S. E. 11 Dr.	0.4	11.7392	0.1360	1.15	0.735	42	M. W.	8	++++	++++ 0.2 c.c.	5555431000	++++	23 yr.	Paresis. Sent to institution.
J. F.	380	52	9 S. E. 2 Dr.	0.4	15.6991	0.1728	1.10	0.57	40	M. W.	10	++++	++++ 0.4 c.c.	5555553210	++++	27 yr.	Paresis; clinical symptoms.
J. F.	487	54	9 S. E. 4 Dr.	0.4	7.3265	0.0837	1.14	0.59	40	M. W.	10	++++	++++ 0.4 c.c.	5555553210	++++	27 yr.	Paresis; clinical symptoms.
J. F.	1472	58	9 S. E. 8 Dr.	0.4	4.9438	0.0490	0.99	2.04	40	M. W.	10	++++	++++ 0.2 c.c.	5555553210	++++	27 yr.	Paresis; clinical symptoms.
N. L.	1343	8	1 Dr.	0.3	7.1970	0.0782	1.08	2.55	24	M. W.	20	+++	++++ 1.0 c.c.	1122100000	+	5 yr.	C. S. L.; clinical symptoms. Had 2 injections in 3 days preceding drainage.
R. E.	1226	7	1 Dr.	0.4	11.0012	0.1165	1.06	0.85	50	M. W.	48	++++	++++ 0.4 c.c.	5555431000	++++	11 yr.	Paresis; clinical symptoms. Had 3 daily I. V.s before drainage.
S. M.	1674	28	14 S. E. 1 Dr.	0.4	4.4473	0.0399	0.89	5.01	42	M. W.	2	Neg.	++++ 0.8 c.c.	1122100000	++++	16 yr.	Early Tabes.
S. M.	1764	29	14 S. E. 2 Dr.	0.4	6.2650	0.0709	1.13	0	42	M. W.	4	Neg.	++++ 0.8 c.c.	1122100000	++++	16 yr.	Early Tabes.
S. M.	2321	32	14 S. E. 5 Dr.	0.4	11.9490	0.1196	1.00	5.57	42	M. W.	2	Neg.	++++ 0.8 c.c.	1122100000	++++	16 yr.	Early Tabes.
S. M.	2891	33	14 S. E. 6 Dr.	0.4	5.9947	0.0666	1.11	18.7	42	M. W.	2	Neg.	++++ 0.8 c.c.	1122100000	++++	16 yr.	Early Tabes.

INTERVAL—3 HOURS

C. B.	2607	24	5 S. E. 11 Dr.	0.4	11.7211	0.1314	1.12	Trace	42	M. W.	10	++	++++ 0.2 c.c.	5555543100	++++	20 yr.	Optic atrophy; paresis. In institution.
J. F.	599	56	9 S. E. 6 Dr.	0.4	13.0124	0.1491	1.14	6.70	40	M. W.	6	++++	++++ 0.2 c.c.	5555553210	++++	27 yr.	Paresis; clinical symptoms.

TABLE I—Continued

TERTIARY LUES—Continued

INTERVAL—4 HOURS

PATIENT	SERIAL NO.	NO. PREVIOUS I. V. INJEC.	NO. PREVIOUS I. S. AND DRAINAGES	DOSE OF DRUG (SAL.)	WT. OF SPECIMEN		PER CENT SOLIDS	AS. IN MG. PER 100 GMS. DRIED SPEC.	AGE	SEX AND COLOR	SPINAL FLUID FINDINGS				BLOOD WASS.	DURATION OF INFECTION	DIAGNOSIS AND REMARKS
					MOIST	DRY					CELLS	GLOB.	WASSERMANN	GOLD SOL			
J. F.	355	51	9 S. E. 1 Dr.	0.4	7.0863	0.0777	1.09	3.86	40	M. W.	10	++++	++++ 0.2 c.c.	5555553210	++++	27 yr.	Paresis; clinical symptoms.
J. F.	579	55	9 S. E. 5 Dr.	0.4	16.4290	0.1780	1.08	0	40	M. W.	8	++++	++++ 0.2 c.c.	5555553210	++++	27 yr.	Paresis; clinical symptoms.

INTERVAL—24 HOURS

PATIENT	SERIAL NO.	NO. PREVIOUS I. V. INJEC.	NO. PREVIOUS I. S. AND DRAINAGES	DOSE OF DRUG (SAL.)	WT. OF SPECIMEN		PER CENT SOLIDS	AS. IN MG. PER 100 GMS. DRIED SPEC.	AGE	SEX AND COLOR	SPINAL FLUID FINDINGS				BLOOD WASS.	DURATION OF INFECTION	DIAGNOSIS AND REMARKS
					MOIST	DRY					CELLS	GLOB.	WASSERMANN	GOLD SOL			
J. M.	2458	17	12 S. E. 5 Dr.	0.4	5.1586	0.0533	1.03	2.81	34	M. W.	Neg.	Neg.	Neg. 2.0 c.c.	1122100000	+++	12 yr.	C. S. L. Had been strongly positive.
T. U. C.	1802	4	0	0.4	7.2699	0.0789	1.08	2.53	45	M. W.	20	++++	++++ 0.8 c.c.	0000000000	++++	2 yr.	C. S. L.; clinical symptoms.
M. C.	359	17	0	0.4	7.4582	0.0881	1.18	3.4	37	F. W.	5	++	++++ 0.6 c.c.	2233210000	++++	8 yr.	C. S. L.; clinical symptoms.
D. D.	1167	9	1 S. E.	0.4	15.3475	0.1712	1.12	1.75	39	M. W.	4	++	++++ 0.4 c.c.	1233210000	++++	8 yr.	C. S. L.; asymptomatic.
S. I. N.	513	9	0	0.4	5.6420	0.0553	0.98	1.82	39	M. W.	10	+++	++++ 0.6 c.c.	1233210000	++++	11 yr.	C. S. L.
W. Y. D.	206	8	0	0.4	13.7867	0.1465	1.06	10.92	40	M. W.	6	Neg.	++++ 0.4 c.c.	1122100000	++++	16 yr.	C. S. L.; clinical symptoms.
W. E.	2888	3	0	0.4	11.8034	0.1379	1.17	2.94	56	M. W.	2	++	++++ 0.2 c.c.	2332100000	++++	15 yr.	Tabes; optic atrophy.
C. L.	421	6	0	0.4	15.0965	0.1515	1.003	1.60	49	M. W.	10	++	++++ 1.5 c.c.	1233210000	++++	25 yr.	Tabes; clinical symptoms.
T. O. R.	209	8	0	0.4	7.8517	0.0858	1.08	8.16	51	F. W.	10	+	++++ 0.4 c.c.	2233210000	Neg.	30 yr.	Tabes; incipient.
C. B.	1757	20	5 S. E. 7 Dr.	0.4	10.7145	0.1138	1.06	26.3	42	M. W.	20	++++	++++ 1.0 c.c.	5555543100	++++	20 yr.	Paresis; optic atrophy.
G. O.	1242	51	29 S. E. 1 Dr.	0.4	7.4265	0.0865	1.16	18.0	36	M. W.	2	++++	++++ 0.8 c.c.	5555542000	++++	10 yr.	Paresis; clinical symptoms. Intensive treatment 3 weeks before.
R. E.	1028	6	0	0.4	2.3247	0.0237	1.01	12.6	50	M. W.	48	++++	++++ 0.4 c.c.	5555431000	++++	11 yr.	Paresis; clinical symptoms.
McG.	1889	26	?	0.3	7.8382	0.0913	1.16	2.73	24	M. W.	2	Trace	++++ 1.0 c.c.	1122100000	Neg.	9 yr.	C. S. L
A .Z.	408	7	0	0.3	4.9263	0.0506	1.02	0.118	53	F. W.	4	Neg.	Neg.	0000000000	++++	2 yr.	For examination only; no symptoms.

INTERVAL—48 HOURS

PATIENT	SERIAL NO.	NO. PREVIOUS I. V. INJEC.	NO. PREVIOUS I. S. AND DRAINAGES	DOSE OF DRUG (SAL.)	WT. OF SPECIMEN		PER CENT SOLIDS	AS. IN MG. PER 100 GMS. DRIED SPEC.	AGE	SEX AND COLOR	SPINAL FLUID FINDINGS				BLOOD WASS.	DURATION OF INFECTION	DIAGNOSIS AND REMARKS
					MOIST	DRY					CELLS	GLOB.	WASSERMANN	GOLD SOL			
F. D.	2712	10	2 S. E.	0.4	11.8588	0.1212	1.02	2.47	23	M. W.		++++	++++ 0.2 c.c.	1232100000	+++	?	C. S. L.
D E.	771	12	0	0.4	14.4150	0.1448	1.004	0.34	23	M. W.	40	++++	++++ 0.1 c.c.	1123210000	++++	3 yr.	C. S. L.; asymptomatic.
J O.	457	4	0	0.4	15.9584	0.1618	1.01	0.308	24	M. W.	18	+	++++ 0.8 c.c.	1233210000	++	?	C. S. L.
L. A. V.	2369	16	6 S. E.	0.4	6.3189	0.0714	1.12	2.80	21	M. W.	Neg.	Neg.	Neg. 2.0 c.c.	0000000000	++++	5 yr.	C. S. L.; had been strongly positive.
C. B.	445	9	1 Dr.	0.4	14.9266	0.1592	1.06	1.20	42	M. W.	10	++	++++ 0.2 c.c.	5555543100	++++	20 yr.	Paresis; optic atrophy. In institution.
C. B.	904	15	5 S. E. 2 Dr.	0.4	14.3915	0.1478	1.02	0.61	42	M. W.	10	++	++++ 0.2 c.c.	5555543100	++++	20 yr.	Paresis; optic atrophy. In institution.
C. B.	983	16	5 S. E. 3 Dr.	0.4	8.7356	0.0934	1.06	1.33	42	M. W.	10	++	++++ 0.2 c.c.	5555543100	++++	20 yr.	Paresis; optic atrophy. In institution.
C B.	1374	18	5 S. E. 5 Dr.	0.4	5.9330	0.0630	1.05	44.4	42	M. W.	20	++++	++++ 0.1 c.c.	5555543100	++++	20 yr.	Paresis; optic atrophy. In institution.

TABLE I—Continued

TERTIARY SYPHILIS—Continued

INTERVAL 48 HOURS—Continued

G. O. L.	1380	52	29 S. E. 2 Dr.	0.4	14.1855	0.1505	1.06	0.66	36	M. W.	48	++++	++++ 0.8 c. c.	5555542000	++++	4 yr.	Paresis; clinical symptoms.
E. D.	2887	1	0	0.4	12.2955	0.1274	1.03	2.35	31	M. W.	10	++	++++ 0.5 c. c.	2223320000	+++	7 yr.	Tabes; advanced.
J. E. N	1079	1	0	0.4	5.3998	0.0506	0.93	11.8	?	M. W.	10	+	++++ 0.2 c. c.	2233210000	Neg.	?	Tabes.
Z. E. L.	370	8	0	0.4	5.2561	0.0578	1.09	0	46	M. W.	5	++	++++ 0.6 c. c.	1233210000	+	24 yr.	Tabes.
E. A.	1665	52	14 S. E. 1 Dr.	0.4	11.6327	0.1215	1.04	0	29	M. W.	6	++	++++ 0.2 c. c.	1233210000	++++	9 yr.	Meningo-vasculitis.
E. E.	1147	11	0	0.4	7.3689	0.0773	1.05	10.3	34	M. W.	48	++++	++++ 0.4 c. c.	2233210000	++++	11 yr.	Optic atrophy.
O. D.	985	53	1 Dr.	0.4	4.3168	0.0422	0.97	35.5	31	M. W.	Neg.	Neg.	Neg.	0000000000	Neg.	8 yr.	No neurosyphilis. Drainage for examination.

INTERVAL—72 HOURS

J. F.	1426	57	9 S. E. 7 Dr.	0.4	7.3230	0.0629	0.858	27.8	40	M. W.	10	++++	++++ 0.2 c.c.	5555553210	++++	24 yr.	Paresis; clinical symptoms.
A. K.	1765	30	16 S. E.	0.3	9.7466	0.0125	1.05	0	34	F. W.	Neg.	Neg.	Neg. 2.0 c.c.	0000000000	Neg.	Unknown	Tabes; had been strongly positive.
O. D.	354	26	0	0.4	6.2410	0.0608	0.97	0	31	M. W.	3	Neg.	Neg. 2.0 c.c.	0000000000	Neg.	8 yr.	No neurosyphilis. Drainage for examination.
R. U.	1345	27	7 S. E.	0.4	7.6190	0.0978	1.28	10.2	22	M. W.	Neg.	Neg.	Neg. 2.0 c.c.	0000000000	Neg.	3 yr.	Cured case. Had had headache and strongly positive fluid 6 months after infection.
P. A.	2714	19	0	0.4	10.1006	0.1010	0.99	0	40	M. W.	10	++++	++++ 0.6 c.c.	1223322100	++++	1 yr.	C. S. L.; asymptomatic.

INTERVAL—96 HOURS

E. E.	1270	12	0	0.4	7.4530	0.0800	1.07	Trace	34	M. W.	48	++++	++++ 0.4 c.c.	2233210000	++++	11 yr.	Optic atrophy; advanced.
A. V.	2367	8	0	0.4	5.0927	0.0963	1.89	0	41	M. W.	40	++++	++++ 0.1 c.c.	5555543200	++++	25 yr.	Tabo-paresis.

INTERVAL—120 HOURS

N. L.	2456	19	9 S. E. 1 Dr.	0.4	7.4953	0.0826	1.09	6.05	24	M. W.	5	Trace	+++ 2.0 c.c.	1122100000	+	5 yr.	C. S. L.; asymptomatic.
B. L.	2368	7	1 Dr.	0.3	4.2026	0.0452	1.07	13.2	38	F. W.	48	++++	++++ 0.1 c.c.	5555543200	++++	Unknown	Paresis; clinical symptoms.
P. A. R.	2515	5	0	0.3	1.9780	0.0184	0.93	54.3	27	F. B.	Neg.	Neg.	Neg. 2.0 c.c.	0000000000	++++	1½ yr.	No neurosyphilis. Drainage for fluid examination.
R. O. S.	2379	13	0	0.4	3.7829	0.0446	1.17	22.47	25	M. W.	Neg.	Neg.	Neg. 2.0 c.c.	0000000000	Neg.	2 yr.	No neurosyphilis. Drainage for fluid examination.

INTERVAL—4 MONTHS

E. C.	362	6	1 Dr.	0.4	5.0070	0.0502	1.002	Trace	49	M. W.	10	++	++++ 1.5 c.c.	1233210000	++++	25 yr.	Tabes; clinical symptoms.
J. F.	446	53	9 S. E. 3 Dr.	0.4	14.4934	0.1538	1.06	0.65	40	M. W.	16	++	++++ 0.2 c.c.	5555532100	++++	27 yr.	Paresis; clinical symptoms.

TABLE II

DETAILED ANALYSIS OF TABLE I, ARRANGED ACCORDING TO TIME INTERVAL WITH THE NUMBER OF CASES IN EACH GROUP WITH BLOOD AND SPINAL FLUID WASSERMANN, NUMBER OF PREVIOUS INTRAVENOUS AND INTRASPINAL INJECTIONS AND DOSE OF DRUG, TOGETHER WITH THE HIGHEST ARSENIC VALUE, THE LOWEST ARSENIC VALUE, AND THE AVERAGE AMOUNT FOUND IN EACH GROUP

INTERVAL—1½ HOURS

II SYPHILIS: 1 case; blood Wassermann strongly positive; spinal fluid negative.

Amount of arsenic: 5.5 mg. after 0.4 gm.; 10 I.V.'s previously; male, white, aged 35; no neurosyphilis; drainage for examination only.

INTERVAL—24 HOURS

II SYPHILIS: 1 case; blood and spinal fluid negative.

Amount of arsenic: Trace after 0.4 gm. and 8 I.V.'s previously; male, white, aged 18; no neurosyphilis; drainage for examination only.

INTERVAL—48 HOURS

II SYPHILIS: 2 cases: blood Wassermann strongly positive in one case; negative in one case; spinal fluid negative in both cases.

Smaller amount of arsenic: Trace after 0.4 gm. and 2 I.V.'s previously, male; white; aged 25; no neurosyphilis; drainage for examination only.

Larger amount of arsenic: 15.2 mg. after 0.4 gm. and 14 I.V.'s previously; male; white; aged 27; no neurosyphilis; drainage for examination only.

Average amount of arsenic in this group: 7.6 mg.

INTERVAL—96 HOURS

II SYPHILIS: 1 case; blood Wassermann positive; spinal fluid negative.

Amount of arsenic: 7.40 mg. after 0.3 gm. and 9 I.V.'s previously; male; white; aged 29; no neurosyphilis; drainage for examination only.

INTERVAL—1 HOUR

III SYPHILIS: 1 case; blood and spinal fluid Wassermann strongly positive.

Amount of arsenic: 1.50 mg. after 0.4 gm.; 11 I.V.'s, and 4 I.S.'s and 5 drainages previously; male; white; aged 42; paresis.

INTERVAL—2 HOURS

III SYPHILIS: 20 cases; blood Wassermann positive in all.

Spinal fluid positive with amounts varying from 0.6—1.0 c.c. in 6 cases, and 0.4—0.2 c.c. in 14 cases.

Number of previous injections: 7—58 I.V.'s; 1-9 I.S.'s; 1—11 drainages.

Dose: 0.3 gm., 1 case; 0.4 gm., 19 cases.

Smallest amount of arsenic: 0 in 5 cases; diagnoses in these cases were as follows; paresis, 4 cases; tabes, 1 case.

TABLE II—Cont'd.

Largest amount of arsenic: 18.7 mg. after 0.4 gm.; 33 I.V.'s, 14 I.S.'s and 6 drainages previously; male; white; aged 42; early tabes.

Average amount of arsenic in this group: 3.18 mg.

INTERVAL—3 HOURS

III SYPHILIS: 2 cases; blood and spinal fluid Wassermann positive.

Smaller amount of arsenic: Trace after 0.4 gm.; 24 I.V.s; 5 I.S.s and 11 drainages previously; male; white; aged 42; paresis.

Larger amount of arsenic: 6.70 mg. after 0.4 gm.; 56 I.V.s; 9 I.S.s and 6 drainages previously; male; white; aged 40; paresis.

Average amount of arsenic in this group: 3.35 mg.

INTERVAL—4 HOURS

III SYPHILIS: 2 cases (same patient) blood and spinal fluid Wassermann strongly positive.

Smaller amount of arsenic: 0 after 0.4 gm., 55 I.V.'s, 9 I.S.'s and 5 drainages previously; male; white; aged 40; paresis.

Larger amount of arsenic: 3.86 mg. after 0.4 gm.; 51 I.V.'s, 9 I.S.'s and one drainage previously; male; white; aged 40; paresis.

Average amount of arsenic in this group: 1.93 mg.

INTERVAL—24 HOURS

III SYPHILIS: 14 cases; blood Wassermann negative in 2, positive in 12 cases.

Spinal fluid negative in 2 cases; positive with amounts varying from 1.0—1.5 c.c. in 3 cases; 0.6-1.0 c.c. in 4 cases; 0.4-0.2 c.c. in 5 cases.

Number of previous injections 3-51 I.V.s; 0-29 I.S.'s; 0.7 drainages.

Dose: 0.3 gm., 2 cases; 0.4 gm., 12 cases.

Smallest amount of arsenic: 0.118 mg. after 0.3 gm. and 7 I.V.s previously; female; white; aged 53; no neurosyphilis, drainage for examination only.

Largest amount of arsenic: 26.3 mg. after 0.4 gm.; 20 I.V.'s, 5 I.S.'s; and 7 drainages previously; male; white; aged 42; paresis.

Average amount of arsenic in this group: 6.84 mg.

INTERVAL—48 HOURS

III SYPHILIS: 15 cases; blood Wassermann negative in 2, positive in 13 cases.

Spinal fluid negative in 2 cases; positive with amounts varying from 0.5-0.8 c.c. in 4 cases; 0.4-0.2 in 9 cases.

Number of previous injections: 1-53 I.V.'s; 0-29 I.S.'s; 0-5 drainages.

Dose: 0.4 gm.

Smallest amount of arsenic: 0 in 2 cases; one after 0.4 gm. and 8 I.V.s previously; male; white; aged 46; tabes.

The other after 0.4 gm.; 52 I.V.s 14 I.S.s and 1 drainage previously; male; white; aged 29; meningovasculitis.

TABLE II—Cont'd.

Largest amount of arsenic: 44.4 mg. after 0.4 gm., 18 I.V.'s, 5 I.S.'s and 5 drainages previously; male; white; aged 42; paresis.

Average amount of arsenic in this group: 4.94 mg.

INTERVAL—72 HOURS

III SYPHILIS: 5 cases; blood negative in 3, positive in 2.

Negative spinal fluid in 3 cases; positive with 0.2 c.c. in 1 case, with 0.4 c.c. in 1 case.

Number of previous injections: 19-57 I.V.s; 9-16 I.S.s; 0-7 drainages.

Dose: 0.3 gm., in one case; 0.4 gm., four cases.

Smallest amount of arsenic: 0 in 3 cases; the first after 0.3 gm.; 30 I.V.s; 16 I.S.s previously; female; white; aged 34; tabes; the second after 0.4 gm. and 26 I.V.s previously; male; white; aged 31; no neurosyphilis, drainage for examination. The third after 0.4 gm. and 19 I.V.s previously; male; white; aged 40; C.S.L.

Largest amount of arsenic: 27.8 mg. after 0.4 gm., 57 I.V.'s, 9 I.S.'s and 7 drainages previously; male; white; aged 40; paresis.

Average amount of arsenic in this group: 7.6 mg.

INTERVAL—96 HOURS

III SYPHILIS: 2 cases; blood and spinal fluid positive in both.

Smaller amount of arsenic: 0 after 0.4 gm. and 8 I.V.s previously; male; white; aged 48; optic atrophy.

Larger amount of arsenic: trace after 0.4 gm., and 8 I.V.s previously; male; white; aged 41; tabo-paresis.

Average amount of arsenic in this group: 0 mg.

INTERVAL—120 HOURS

III SYPHILIS: 4 cases; blood negative in 1; positive in 3 cases.

Spinal fluid negative in 2 cases, positive with 0.1 c.c. 1 case and with 2.0 c.c. 1 case.

Number of previous injections: 5-19 I.V.s; 0-10 I.S.s.

Dose: 0.3 gm. in two cases; 0.4 gm. in two cases.

Smallest amount of arsenic: 6.05 mg. after 0.4 gm.; 19 I.V.s; 9 I.S.s and 1 drainage previously; male; white; aged 24; C.S.L.

Largest amount of arsenic: 54.3 mg. after 0.3 gm. and 5 I.V.s previously; female; black; aged 27; no neurosyphilis, drainage for examination.

Average amount of arsenic in this group: 24.0 mg.

INTERVAL—4 MONTHS

III NEUROSYPHILIS: 2 cases; blood and spinal fluid positive in both.

Smallest amount of arsenic: trace after 0.4 gm. and six I.V.s and one drainage; male; white; aged 49; tabes.

Largest amount of arsenic: 0.65 mg. after 0.4 gm. 53 I.V.'s, 9 I.S.'s and 3 drainages previously; male; white; aged 40; paresis.

Average amount of arsenic in this group: 0.33 mg.

TABLE III

CLASSIFIED ACCORDING TO QUANTITY OF ARSENIC PRESENT IN THE CEREBROSPINAL FLUID AND CLINICAL DIAGNOSIS

		O ARSENIC		
Tabes	Serial No.	1764	2 Hr.	
		370	48 “	
		1765	72 “	
Paresis		1528	2 “	
		1998	“ “	
		1004	“ “	
		1081	“ “	
		579	4 “	
		2367	96 “	
C.S.L.		1665	48 “	
		2714	72 “	
Syphilitic Infection without C.N.S. Involvement		354	72 “	
		INDETERMINATE AMOUNTS OF ARSENIC		
Tabes	Serial No.	362	4 Mo.	
Optic Atrophy		1270	96 Hr.	
Paresis		1882	2 “	
		2607	3 “	
Syphilitic Infection without C.N.S. Involvement		989	24 “	
		1265	48 “	
		0.118 MG.-.5 MG. ARSENIC PER 100 GM. DRIED SPEC.		
Tabes	Serial No.	2888	24 Hr.	2.94 mg.
		421	“ “	1.60 “
		2887	48 “	2.35 “
Paresis		1096	2 “	1.50 “
		1666	“ “	1.41 “
		1768	“ “	3.15 “
		1847	“ “	3.59 “
		1881	“ “	0.735 “
		380	“ “	0.57 “
		487	“ “	0.59 “
		1472	“ “	2.04 “
		1343	“ “	2.55 “
		1226	“ “	0.85 “
		355	4 “	3.86 “
		445	48 “	1.20 “
		904	“ “	0.61 “
		983	“ “	1.33 “
		1380	“ “	0.66 “
		446	4 Mo.	0.65 “
C.S.L.		2458	24 Hr.	2.81 “
		1802	“ “	2.53 “
		359	“ “	3.4 “
		1167	“ “	1.75 “

TABLE III—Cont'd.

0.118 MG.-5.0 MG. ARSENIC PER 100 GM. DRIED SPEC.

C.S.L.	Serial No. 513	24 Hr.	1.82 mg.
	2712	48 “	2.47 “
	771	“ “	0.34 “
	457	“ “	0.308 “
	2369	“ “	2.80 “
	1889	24 “	2.73 “
Syphilitic Infection without C.N.S. Involvement	408	“ “	0.118 “

5 MG.-20 MG. OF ARSENIC PER 100 GM. DRIED SPEC.

Tabes	Serial No. 1674	2 Hr.	5.01 mg.
	2321	“ “	5.57 “
	2891	“ “	18.7 “
	209	24 “	8.16 “
	1079	48 “	11.8 “
Optic Atrophy	1147	48 “	10.3 “
Paresis	1169	2 “	9.50 “
	1267	“ “	9.3 “
	599	3 “	6.70 “
	1242	24 “	18.0 “
	1028	“ “	12.6 “
	2368	120 “	13.2 “
C.S.L.	206	24 “	10.92 “
	2456	120 “	6.05 “
Syphilitic Infection without C.N.S. Involvement	986	1½ “	5.5 “
	1850	48 “	15.2 “
	2365	96 “	7.4 “
Cured Case	1345	72 “	10.2 “

20 MG.-54.3 MG. ARSENIC PER 100 GM. DRIED SPEC.

	Serial No. 1757	24 Hr.	26.3 mg.
Paresis		48 “	44.4 “
	1374	72 “	27.8 “
	1426		
Syphilitic Infection without C.N.S. Involvement		48 “	35.5 “
	985	120 “	54.3 “
	2515	“ “	22.47 “
	2379		

SUMMARY

1. This paper covers the results of our investigations of the cerebrospinal fluid for arsenic content after intravenous injection of salvarsan and simple drainage.

2. For this study 40 patients were utilized and 72 fluids examined.

3. The clinical diagnoses were as follows: 9 cases of secondary and tertiary syphilis without involvement of the central nervous system; 14 cases of cerebrospinal syphilis; 8 cases of tabes (1 with

optic atrophy); 8 cases of paresis (1 with optic atrophy); and 1 case of simple optic atrophy.

4. In Table I will be found the serological and clinical findings at the time the arsenic analyses were made on each fluid.

5. The time intervals at which the specimens were taken after the intravenous injections are charted in Table I.

6. Table I also records, under their respective headings, the size of the specimen, percentage solids, and the amount of arsenic in milligrams per 100 grams of dry specimen.

7. Table II is an analysis of Table I, giving time intervals, number of cases in each group, serology and previous treatment, together with the highest arsenic value, lowest arsenic value and the average quantity found in each group.

8. Table III classifies the data on a quantitative and clinical basis in the following 5 groups:

1. "No arsenic," 17 per cent of the cerebrospinal fluids: tabes 4.2 per cent; paresis 8.3 per cent; cerebrospinal syphilis 2.8 per cent; syphilitic infection without involvement of the central nervous system 1.4 per cent.

2. "Indeterminate amounts of arsenic"; 8.3 per cent of the cerebrospinal fluids: tabes 1.4 per cent; optic atrophy 1.4 per cent; paresis 2.8 per cent; syphilitic infection without involvement of the central nervous system 2.8 per cent.

3. "From 0.118 mg. to 5 mg. arsenic per 100 grams dried specimen"; 41.7 per cent of the cerebrospinal fluids: tabes 4.2 per cent; paresis 22 per cent; cerebrospinal syphilis 14 per cent; syphilitic infection without involvement of the central nervous system 1.4 per cent.

4. "From 5 mg. to 20 mg. per 100 grams dried specimen"; 25 per cent of the cerebrospinal fluids: tabes 7 per cent; optic atrophy 1.4 per cent; paresis 8.4 per cent; cerebrospinal syphilis 2.8 per cent; syphilitic infection without involvement of the central nervous system 4.2 per cent; cured cases 1.4 per cent.

5. "From 20 mg. to 54.3 mg. per 100 gm. dried specimen"; 8.4 per cent of the cerebrospinal fluids: paresis 4.2 per cent; syphilitic infection without involvement of the central nervous system 4.2 per cent.

9. A clinical discussion and interpretation will follow at the close of this series of papers.

QUANTITATIVE STUDIES IN SYPHILIS FROM A CLINICAL AND BIOLOGICAL POINT OF VIEW

VIII. The Arsenic Content of the Blood after Intravenous Injection of Silver Salvarsan

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THESE studies on silver salvarsan parallel those made with the preparations salvarsan and neosalvarsan. With a few exceptions the 214 patients on whom these investigations were made were syphilitics representing all stages of the disease; 299 specimens of blood were analyzed. The average weight of these patients was about 60 kilograms and the average dose of the drug 0.25 grams. As there are about 85 c.c. of blood for each kilogram of body weight, the total amount for each patient would be 5100 c.c. The average percentage of solids in round figures is 22, or 1122 grams of total solids per patient.

In 0.25 grams of silver salvarsan there are 52.1 mg. of metallic arsenic. Therefore, if all of the arsenic remained in the blood stream there would be 4.65 mg. of metallic arsenic per 100 grams of dried specimen. (The reader is referred to articles I and V for a fuller discussion of the method of calculation.)

The silver salvarsan was prepared by dissolving the drug in the proportion of 0.1 gram in 5 c.c. of sterile distilled water. The solution was then diluted with cool, sterile freshly prepared saline solution of about 0.4 per cent, made from chemically pure sodium chloride so that the final dilution of the drug is in the proportion of 0.1 gram to 20 c.c. of solution. After filtering, the preparation is injected by the gravity method. The average dose administered was 0.25 grams of a product which contained 20.83 per cent arsenic.

The following Tables give the data relating to these analyses:

EXPLANATIONS OF ABBREVIATIONS USED IN TABLES

I. V. = Intravenous injection
I. S. = Intraspinal injection
Dr. = Drainage
S. E. = Swift-Ellis method of intraspinal treatment
S. F. = Spinal Fluid
S.; Sal.; Salv. = Salvarsan
S. S. = Silver Salvarsan
Neo. = Neosalvarsan
Glob. = Globulin
Wass. = Wassermann
I = Primary Syphilis
II = Secondary Syphilis
III = Tertiary Syphilis
C. S. L. = Cerebro-spinal syphilis
G. P. = General paresis

(*Continued on page* 530.)

Table I

Silver Salvarsan Chart

SERIAL NO.	DATE OF LAST INJECTION S. S.	NO. PREV. I. V. INJEC. SALV. NEO & S. S.	DOSE OF DRUG S. S.	TIME AFTER INJECTION	WT. OF SPECIMEN		PER CENT SOLIDS	AS. IN MGS. PER 100 GMS. DRIED SPEC.	AGE	SEX AND COLOR	WASS.	DURATION OF INFECTION	DIAGNOSIS AND REMARKS
					MOIST	DRY							
Interval—Immediate (49 cases)													
2913	1/12/23	13	0.25	0+	4.7167	0.9118	19.33	0.432	50	M. W.	++++	7 yr.	Tertiary syphilis
2939	1/13/23	1	0.25	0+	6.0125	1.1175	18.58	0.089	27	F. B.	++++	?	Tertiary syphilis
2905	1/13/23	0	0.25	0+	5.7806	1.1928	20.63	0.419	26	F. W.	Neg.	?	Non-syphilitic
2961	1/13/23	0	0.2	0+	4.6733	0.9789	20.96	0.816	32	F. B.	++++	?	Tertiary syphilis
2680	12/15/22	64	0.2	0+	7.8055	1.8603	23.83	0.268	70	M. W.	++++	24 yr.	Tabes dorsalis
2922	1/13/23	5	0.25	0+	6.1675	1.3249	21.48	1.15	27	M. W.	++++	9 yr.	Tertiary syphilis
2943	1/13/23	7	0.25	0+	4.2400	0.8895	20.98	0.337	40	F. W.	++++	10 mo.	Tertiary syphilis
2899	1/13/23	21	0.25	0+	5.6502	1.1228	19.87	0.593	25	M. B.	Neg.	2 yr.	Tertiary syphilis
2957	1/13/23	40	0.2	0+	5.4212	1.1834	21.88	0.565	38	F. W.	+++	10 yr.	Tertiary syphilis, Tabes
2924	1/13/23	9	0.25	0+	4.8376	1.0971	22.68	1.82	30	M. W.	+++	?	Tertiary syphilis
2955	1/13/23	5	0.2	0+	5.7379	1.1468	20.00	2.32	30	F. W.	++++	4 mo.	Secondary syphilis
776	10/10/21	4	0.2	0+	6.9252	1.4949	21.60	6.60	23	M. W.	++++	2 mo.	Secondary syphilis
2959	1/12/23	12	0.25	0+	4.6140	0.9967	21.39	0.501	32	M. B.	+	11 yr.	Tertiary syphilis
2933	1/12/23	10	0.2	0+	6.8489	1.3310	19.43	4.51	30	F. B.	++++	?	Tertiary syphilis
2895	1/12/23	1	0.25	0+	4.7893	0.9768	20.39	7.15	37	M. W.	Neg.		Non-syphilitic (epilepsy)
2897	1/12/23	23	0.25	0+	3.6184	0.7688	21.24	7.80	32	M. B.	++++	?	Tertiary syphilis
2926	1/12/23	21	0.2	0+	4.4517	0.9066	20.36	8.82	38	F. W.	+++	?	Tertiary syphilis
2947	1/12/23	14	0.2	0+	5.4650	1.0923	19.97	2.73	37	F. W.	++++	?	Tertiary syphilis
2907	1/12/23	16	0.25	0+	4.9742	0.9519	19.13	4.20	28	M. W.	++++	6 yr.	Tertiary syphilis
2909	1/12/23	11	0.2	0+	4.3579	0.8156	18.71	1.53	33	F. B.	++++	?	Tertiary syphilis
2937	1/12/23	0	0.2	0+	6.2493	1.1008	19.62	4.55	27	F. B.	++++	?	Tertiary syphilis
2949	1/12/23	6	0.25	0+	4.8160	1.0611	22.03	0.942	20	M. B.	++++	2 mo.	Secondary syphilis
2967	1/12/23	0	0.2	0+	3.9732	0.7752	19.51	2.56	16	F. B.	++++	?	Tertiary syphilis
2969	1/12/23	10	0.2	0+	5.7428	0.9934	17.30	1.34	28	F. W.	++++	?	Tertiary syphilis

2941	1/12/23	4	0.2	0+	5.8746	1.0710	18.23	5.60	23	F. B.	++++	3 mo.	Tertiary syphilis
2901	1/12/23	23	0.25	0+	5.5727	1.2503	22.43	2.39	24	M. W.	++++	8 yr.	Tertiary syphilis
2935	1/12/23	2	0.2	0+	5.0976	0.9524	18.68	0.314	24	F. W.	++++	?	Tertiary syphilis
2929	1/12/23	6	0.2	0+	6.4280	1.3320	20.72	10.00	45	M. W.	++++	7 yr.	Tertiary syphilis
2931	1/12/23	7	0.2	0+	5.7770	1.0705	18.52	9.30	40	F. B.	++++	7 yr.	Tertiary syphilis
2965	1/12/23	1	0.2	0+	3.6510	0.8044	22.03	0.310	26	F. W.	++++	2 mo.	Secondary syphilis
2903	1/12/23	30	0.25	0+	5.1252	1.1385	22.21	0.878	34	M. W.	++++	1 yr.	Secondary syphilis
2927	1/12/23	7	0.25	0+	3.7676	0.6840	18.15	7.35	37	M. W.	++++	3 mo.	Secondary syphilis
2963	1/12/23	3	0.2	0+	5.6150	0.9809	17.47	2.71	28	F. B.	++++	?	Tertiary syphilis
2951	1/12/23	12	0.2	0+	5.1900	1.0724	20.66	1.86	38	F. W.	++++	?	Tertiary syphilis
3133	1/24/23	40	0.2	0+	5.9118	1.1148	18.85	7.27	35	F. W.	++++	?	Tertiary syphilis
2920	1/12/23	10	0.25	0+	7.2493	1.4870	20.51	0.201	22	M. W.	++++	3 yr.	Tertiary syphilis
2953	1/12/23	20	0.2	0+	5.6740	1.0676	18.96	1.87	29	F. W.	++++	4 yr.	Tertiary syphilis
2911	1/12/23	2	0.25	0+	4.1434	0.8479	20.46	0.588	28	M. W.	+++	6 wk.	Secondary syphilis
2893	1/12/23	3	0.25	0+	7.0697	1.3875	19.62	1.80	30	M. B.	++++	?	Tertiary syphilis
809	10/21/21	7	0.2	0+	6.3979	1.2942	20.23	0.308	18	F. W.	++++	3 mo.	Secondary syphilis
2917	1/12/23	13	0.25	0+	5.4889	1.1775	21.45	1.69	27	M. W.	Neg.	6 mo.	Secondary syphilis
2915	1/12/23	90	0.25	0+	5.6130	0.8739	15.56	0.835	35	M. W.	+	14 yr.	C. S. L.
2945	1/12/23	44	0.2	0+	4.9835	0.9794	19.68	2.55	29	F. W.	Neg.	7 yr.	Neurosyphilis
3287	2/ 8/23	20	0.2	0+	4.9100	0.9110	18.55	0.926	40	F. W.	+++	18 yr.	C. S. L.
2973	1/13/23	6	0.2	0+	7.3035	1.6093	22.04	0.219	50	M. W.	++++	unknown	Latent syphilis
3158	1/27/23	7	0.2	0+	7.2907	1.6107	22.09	0.496	50	M. W.	++++	unknown	Latent syphilis
3277	2/ 9/23	15	0.2	0+	3.3339	0.6860	20.60	0.869	28	M. W.	Neg.	1 yr.	Secondary syphilis
2877	1/11/23	4	0.2	0+	7.1655	1.6218	22.63	4.11	42	M. W.	Neg.	20 yr.	Optic atrophy.
3227	2/ 3/23	20	0.2	0+	6.3265	1.2160	19.22	2.05	45	F. W.	+++	26 yr.	C. S. L.

Interval—5 minutes (24 cases)

3105	1/29/23	0	0.25	5 m.	4.5576	1.0192	22.30	0.326	31	M. W.	+++	10 yr.	Tertiary syphilis
3099	1/29/23	2	0.2	5 m.	5.3270	1.0921	20.50	0.454	25	F. W.	++++	?	Tertiary syphilis
2824	1/ 8/23	30	0.25	5 m.	4.7777	0.9441	19.76	0.317	26	F. W.	++++	?	Tertiary syphilis
3655	3/23/23	21	0.25	5 m.	7.6495	1.5260	19.94	2.62	25	M. B.	++	2 yr.	Tertiary syphilis
3107	1/29/23	30	0.2	5 m.	5.5297	1.0805	19.54	1.45	25	F. W.	++++	10 yr.	Latent syphilis
3657	3/23/23	1	0.2	5 m.	6.2365	1.1600	18.59	3.44	29	F. B.	++++	?	Tertiary syphilis
3103	1/29/23	1	0.25	5 m.	6.5646	1.3393	20.40	1.50	20	M. W.	Neg.	——	Non-syphilitic

TABLE I—Continued

SERIAL NO.	DATE OF LAST INJECTION S. S.	NO. PREV. I. V. INJEC. SALV. NEO & S. S.	DOSE OF DRUG S. S.	TIME AFTER INJECTION	WT. OF SPECIMEN		PER CENT SOLIDS	AS. IN MGS. PER 100GMS. DRIED SPEC.	AGE	SEX AND COLOR	WASS.	DURATION OF INFECTION	DIAGNOSIS AND REMARKS
					MOIST	DRY							
Interval—5 minutes (24 cases)—Continued													
3131	1/24/23	0	0.25	5 m.	6.0259	1.2286	20.38	2.22	46	M. B.	++++	4 yr.	Tertiary syphilis
3127	1/26/23	12	0.2	5 m.	4.9201	1.0101	20.53	1.71	27	F. W.	++++	6 mo.	Tertiary syphilis
2388	10/27/22	14	0.2	5 m.	5.4461	1.2026	22.08	0.277	42	M. W.	+	21 yr.	Tertiary syphilis
3104	1/29/23	15	0.25	5 m.	5.4905	1.1016	20.06	1.81	37	M. W.	Neg.	10 yr.	Tertiary syphilis
3126	1/24/23	28	0.25	5 m.	4.7671	0.9386	19.68	3.20	55	M. W.	++++	25 yr.	Tertiary syphilis
3656	3/23/23	5	0.25	5 m.	5.8697	1.1897	20.09	3.36	34	M. W.	+	?	Tertiary syphilis
3130	1/24/23	21	0.2	5 m.	5.6816	0.9481	16.69	1.70	20	F. B.	Neg.	1 yr.	Secondary syphilis
3125	1/24/23	34	0.2	5 m.	7.4515	1.5818	21.22	2.08	35	F. W.	++	?	Tertiary syphilis
3139	1/26/23	0	0.25	5 m.	6.5959	1.3493	22.12	0.074	20	M. W.	++++	3 yr.	Tertiary syphilis
2797	1/ 5/23	14	0.2	5 m.	7.1602	1.5913	22.20	0.062	50	M. W.	Neg.	14 mo.	Secondary syphilis
2982	1/11/23	17	0.25	5 m.	5.9879	1.1110	18.55	0.045	40	F. W.	+++	18 yr.	C. S. L.
2380	10/24/22	5	0.2	5 m.	7.8676	1.6365	20.80	0.611	35	M. W.	++++	12 yr.	Paresis
2980	1/12/23	6	0.2	5 m.	6.5161	1.3137	20.16	1.52	35	M. W.	++++	20 yr.	C. S. L.
2875	1/ 9/23	5	0.2	5 m.	5.9724	1.3647	22.85	0.571	67	M. W.	++++	40 yr.	C. S. L.
2979	1/12/23	19	0.2	5 m.	7.5007	1.4507	19.34	0.222	45	F. W.	+++	26 yr.	C. S. L.
2977	1/13/23	6	0.2	5 m.	7.5320	1.5468	20.54	0.259	62	M. W.	++++	32 yr.	C. S. L.
2876	1/10/23	3	0.2	5 m.	8.2297	1.8973	23.05	0.877	44	M. W.	Neg.	24 yr.	Tabes.
Interval—10 minutes (24 cases)													
2827	1/ 8/23	15	0.25	10 m.	4.7827	1.1739	24.54	0.143	21	M. W.	++++	21 yr.	Congenital syphilis
2835	1/ 8/23	49	0.25	10 m.	5.2382	1.1802	22.53	3.40	37	M. W.	++++	10 yr.	Tertiary syphilis
2833	1/ 8/23	6	0.25	10 m.	3.9966	0.7613	19.04	0.132	22	F. W.	++++	8 mo.	Secondary syphilis
2821	1/ 8/23	1	0.2	10 m.	5.8586	1.4383	24.55	0.69	26	F. W.	++++	?	Tertiary syphilis

1330	2/18/21	0	0.2	10 m.	6.5205	1.4835	22.90	0.0339	40	M. W.	++++	20 yr.	Tertiary syphilis
544	7/25/21	12	0.2	10 m.	5.7167	1.2489	21.84	2.08	21	F. W.	++++	1 yr.	Secondary syphilis
2834	1/ 8/23	22	0.25	10 m.	5.3310	1.0401	19.51	1.15	26	F. W.	++++	1 yr.	Secondary syphilis
3134	1/26/23	2	0.2	10 m.	5.2926	0.9844	18.59	0.41	27	B. F.	++++	20 yr.	Tertiary syphilis
2819	1/ 8/23	6	0.25	10 m.	4.7757	0.9321	19.51	0.858	30	F. W.	++++	12 yr.	Tertiary syphilis
882	11/16/21	31	0.3	10 m.	6.8444	1.4386	21.01	0.13	36	F. W.	++++	4 yr.	Tertiary syphilis
3102	1/29/23	4	0.25	10 m.	5.4410	1.1966	21.99	0.4444	29	M. B.	++++	2 mo.	Secondary syphilis
2816	1/ 8/23	0	0.25	10 m.	5.5867	1.1827	21.17	0.33	46	M. B.	++	?	Tertiary syphilis
2815	1/ 8/23	1	0.25	10 m.	6.0925	1.3425	22.03	1.11	28	M. W.	+++	6 wk.	Secondary syphilis
2845	1/10/23	11	0.25	10 m.	4.2720	1.0528	24.62	0.857	31	M. W.	++++	7 mo.	Secondary syphilis
2832	1/ 8/23	10	0.25	10 m.	7.1665	1.6474	22.98	0.182	28	M. W.	++++	8 mo.	Secondary syphilis
548	7/25/21	10	0.2	10 m.		1.0680		1.09	24	F. W.	Neg.	6 mo.	Secondary syphilis
3651	3/23/23	15	0.25	10 m.	6.3650	1.2784	20.08	1.56	45	M. W.	++++	?	Tertiary syphilis
2983	1/12/23	15	0.2	10 m.	8.9410	1.9021	21.16	1.76	50	M. W.	Neg.	14 mo.	Secondary syphilis
2872	1/ 9/23	7	0.2	10 m.	6.0102	1.5488	25.76	2.15	52	M. W.	+++	16 yr.	Latent syphilis
3183	1/31/23	35	0.2	10 m.	7.2363	1.6279	22.49	0.184	62	M. W.	Neg.	30 yr.	C. S. L.
2874	1/10/23	19	0.2	10 m.	5.9507	1.2375	20.78	0.161	45	F. W.	++++	?	C. S. L.
2792	1/ 5/23	11	0.2	10 m.	7.2178	1.5690	21.70	1.27	37	M. W.	++++	10 yr.	Tertiary syphilis
2793	1/ 8/23	20	0.2	10 m.	7.5270	1.6324	21.60	0.245	47	F. W.	Neg.	24 yr.	C. S. L.
3185	1/31/23	22	0.2	10 m.	7.3309	1.5323	20.91	1.31	47	F. W.	Neg.	24 yr.	C. S. L.
Interval—15 minutes (22 cases)													
2837	1/10/23	20	0.25	15 m.	4.6967	0.9719	20.69	0.201	40	F. W.	++++	?	Tertiary syphilis
2840	1/10/23	5	0.25	15 m.	2.3767	0.5273	19.32	0.949	24	F. W.	++++	4 yr.	Tertiary syphilis
2810	1/ 8/23	48	0.25	15 m.	6.2505	1.3897	22.55	1.08	39	M. W.	++++	18 yr.	Tertiary syphilis
2844	1/10/23	9	0.25	15 m.	4.1170	0.9190	22.32	0.931	35	M. B.	++++	3 yr.	Tertiary syphilis
2436	11/ 1/22	8	0.2	15 m.	3.9615	0.8523	21.51	0	43	M. W.	++++	?	Tertiary syphilis
2803	1/ 8/23	3	0.25	15 m.	3.8515	0.8632	22.41	0.1772	20	M. B.	++++	8 mo.	Secondary syphilis
2839	1/10/23	5	0.25	15 m.	6.4209	1.2755	29.86	0.390	30	M. W.	++++	8 mo.	Secondary syphilis
2828	1/ 8/23	20	0.25	15 m.	5.8108	1.3747	23.65	0.220	27	F. W.	++++	2 yr.	Tertiary syphilis
2805	1/ 8/23	0	0.25	15 m.	5.3342	1.1846	22.20	1.12	25	M. B.	++++	3½ yr.	Tertiary syphilis
2826	1/ 8/23	13	0.25	15 m.	5.8539	1.3483	23.03	1.111	37	M. W.	++++	?	Tertiary syphilis
2862	1/10/23	4	0.25	15 m.	5.3383	1.2335	23.08	0.48	30	M. W.	++++	2 mo.	Secondary syphilis
2813	1/ 8/23	16	0.2	15 m.	5.7024	1.2602	22.09	0.590	45	F. W.	++++	20 yr.	Tertiary syphilis

Table I—Continued

SERIAL NO.	DATE OF LAST INJECTION S. S.	NO. PREV. I. V. INJEC. SALV. NEO & S. S.	DOSE OF DRUG S. S.	TIME AFTER INJECTION	WT. OF SPECIMEN		PER CENT SOLIDS	AS. IN MGS. PER 100 GMS. DRIED SPEC.	AGE	SEX AND COLOR	WASS.	DURATION OF INFECTION	DIAGNOSIS AND REMARKS
					MOIST	DRY							
Interval—15 minutes—Continued													
2857	1/10/23	6	0.25	15 m.	4.8133	1.0434	21.67	0.865	21	F. W.	++++	?	Tertiary syphilis
2836	1/10/23	0	0.2	15 m.	5.7852	1.1854	20.49	0.84	30	F. W.	++++	3 mo.	Secondary syphilis
2854	1/10/23	38	0.25	15 m.	7.8300	1.6510	21.09	0.241	25	M. W.	++++	10 yr.	Tertiary syphilis
2866	1/10/23	17	0.25	15 m.	5.0461	1.0527	20.86	1.90	27	M. W.	++++	6 mo.	Secondary syphilis
2849	1/10/23	6	0.25	15 m.	5.7566	1.2249	21.28	0.164	29	M. B.	++++	4 yr.	Tertiary syphilis
3181	2/ 1/23	19	0.2	15 m.	7.8511	1.5445	19.67	0.216	40	F. W.	+++	18 yr.	C. S. L.
2795	1/ 5/23	9	0.2	15 m.	9.4239	1.9664	20.80	0.050	58	M. W.	Neg.	?	Neuro-syphilis
3225	2/ 2/23	3	0.2	15 m.	7.3533	1.4715	20.01	0	28	M. W.	Neg.	1 yr.	Secondary syphilis
3024	1/16/23	21	0.15	15 m.	7.6016	1.5058	19.98	0.993	47	F. W.	Neg.	24 yr.	C. S. L.
3025	1/16/23	15	0.2	15 m.	7.6344	1.5193	19.90	0.395	70	M. W.	++	15 yr.	Tertiary syphilis
Interval—20 minutes (19 cases)													
2822	1/ 8/23	56	0.25	20 m.	5.9771	1.3984	23.39	0.510	34	M. W.	++++	14 yr.	C. S. L.
2859	1/10/23	5	0.25	20 m.	3.2917	0.7700	23.39	0.372	39	M. W.	Neg.	2 yr.	C. S. L.
2811	1/ 8/23	34	0.25	20 m.	5.5776	1.1412	20.46	0.525	33	F. W.	++++	?	Tertiary syphilis
2858	1/10/23	7	0.25	20 m.	5.4606	1.2232	22.40	0.082	29	M. W.	++++	6 mo.	Secondary syphilis
2855	1/10/23	8	0.25	20 m.	6.0683	1.2300	20.26	0.407	30	F. W.	++++	?	Tertiary syphilis
2806	1/ 8/23	53	0.25	20 m.	6.6945	1.3206	19.72	0.946	32	F. W.	++++	?	C. S. L.
2868	1/10/23	6	0.25	20 m.	4.9717	1.1920	23.97	0	39	F. W.	++++	22 yr.	Paresis
2831	1/ 8/23	2	0.25	20 m.	7.2393	1.5948	22.02	0.184	30	F. W.	++	?	Tertiary syphilis
2829	1/ 8/23	7	0.25	20 m.	5.0271	1.0465	20.81	0.381	27	M. W.	++++	?	Secondary syphilis
2847	1/10/23	0	0.25	20 m.	5.9279	1.2594	21.24	0.317	51	M. B.	++++	?	Tertiary syphilis
2818	1/ 8/23	21	0.25	20 m.	5.6060	1.2267	21.88	0.168	28	F. W.	++++	?	Tertiary syphilis

2825	1/ 8/23	54	0.25	20 m.	5.1159	1.1903	23.26	1.008	26	F. W.	++++	2½ yr.	Tertiary syphilis
2842	1/10/23	10	0.2	20 m.	4.6145	1.0148	21.99	0.798	39	M. B.	++++	?	Secondary syphilis
3187	1/30/23	6	0.2	20 m.	7.5903	1.6327	21.51	0.781	42	M. W.	Neg.	20 yr.	Optic atrophy
3018	1/16/23	5	0.2	20 m.	6.7993	1.4058	20.68	1.06	42	M. W.	Neg.	20 yr.	Optic atrophy
3275	2/ 5/23	40	0.2	20 m.	8.2468	1.6569	20.09	0.47	39	M. W.	++++	Denied	Optic atrophy. Paresis
3407	2/28/23	24	0.2	20 m.	6.4290	1.3710	21.32	0.438	47	F. W.	Neg.	24 yr.	C. S. L.
3266	2/ 6/23	23	0.2	20 m.	6.7406	1.3821	20.51	0.136	47	F. W.	Neg.	24 yr.	C. S. L.
3229	2/ 2/23	26	0.2	20 m.	8.0540	1.7532	21.76	0.408	42	M. W.	Neg.	23 yr.	Tabes

Interval—25 minutes (6 cases)

2838	1/10/23	17	0.25	25 m.	7.2265	1.4308	18.41	0.840	41	M. W.	++++	?	Tabes
2867	1/10/23	30	0.25	25 m.	4.2113	0.8963	21.28	1.39	28	F. B.	+++	?	Tertiary syphilis
2820	1/ 8/23	21	0.25	25 m.	5.7501	1.3494	23.44	0.222	25	M. B.	+++	6 yr.	Tertiary syphilis
2848	1/10/23	15	0.25	25 m.	5.0112	1.0702	21.35	0.187	32	M. W.	Neg.	6 mo.	Secondary syphilis
2802	1/ 8/23	2	0.2	25 m.	5.5914	1.0885	19.46	0.046	25	F. W.	++++	?	Tertiary syphilis
2846	1/10/23	4	0.25	25 m.	5.2535	1.1396	21.68	1.755	37	M. W.	++++	2½ yr.	Tertiary syphilis

Interval—30 minutes (21 cases)

2843	1/10/23	60	0.25	30 m.	4.8472	1.1171	23.03	0	30	M. W.	+++	?	Tertiary syphilis
2852	1/10/23	4	0.25	30 m.	5.3683	1.2060	22.46	1.00	33	M. W.	Neg.	4 wk.	Primary syphilis
2841	1/10/23	7	0.25	30 m.	9.4474	2.0954	22.17	1.24	25	M. B.	Neg.	5 wk.	Primary syphilis
3138	1/26/23	14	0.2	30 m.	4.2629	0.9272	21.75	5.37	33	F. W.	++++	?	Tertiary syphilis
2865	1/10/23	5	0.2	30 m.	6.2141	1.3489	21.70	0.222	31	M. B.	++++	3 yr.	Tertiary syphilis
883	11/16/21	31	0.3	30 m.	4.9998	1.0880	21.76	0.73	36	F. W.	++++	4 yr.	Tertiary syphilis
2856	1/10/23	6	0.2	30 m.	4.2584	0.8889	20.87	1.12	49	M. B.	++++	20 yr.	Tertiary syphilis
549	7/25/21	10	0.2	30 m.	7.6649	1.5532	20.26	0.225	24	F. W.	Neg.	6 mo.	Secondary syphilis
2809	1/ 8/23	1	0.2	30 m.	6.0955	1.2430	20.39	0.0402	26	F. B.	++++	?	Tertiary syphilis
2823	1/ 8/23	18	0.25	30 m.	4.3603	0.8810	20.20	0.908	42	M. W.	++++	20 yr.	G. P. Optic atrophy.
2851	1/10/23	3	0.25	30 m.	7.3205	1.7737	24.22	0.452	37	M. B.	++++	2 yr.	Tertiary syphilis
2808	1/ 8/23	72	0.25	30 m.	7.8672	1.8157	23.08	0.165	40	M. W.	++++	20 yr.	Optic atrophy
2804	1/ 8/23	4	0.2	30 m.	5.1766	0.9388	18.13	0	35	F. W.	++++	6 mo.	Secondary syphilis
2807	1/ 8/23	9	0.25	30 m.	4.5657	1.0217	22.37	1.22	40	M. B.	++++	7 yr.	Tertiary syphilis
2830	1/ 8/23	1	0.25	30 m.	6.5329	1.4702	22.35	0.34	38	F. B.	++++	?	Tertiary syphilis
2814	1/ 8/23	0	0.25	30 m.	5.2389	1.1733	22.39	1.70	26	F. W.	++++	2 mo.	Secondary syphilis
2796	1/ 5/23	5	0.2	30 m.	5.9305	1.3129	22.10	0	35	M. W.	++++	20 yr.	C. S. L.

TABLE I—Continued

SERIAL NO.	DATE OF LAST INJECTION S. S.	NO. PREV. I. V. INJEC. SALV. NEO & S. S.	DOSE OF DRUG S. S.	TIME AFTER INJECTION	WT. OF SPECIMEN		PER CENT SOLIDS	AS. IN MGS. PER 100GMS. DRIED SPEC.	AGE	SEX AND COLOR	WASS.	DURATION OF INFECTION	DIAGNOSIS AND REMARKS
					MOIST	DRY							
Interval—30 minutes—Continued													
2794	1/ 6/23	18	0.125	30 m.	6.6632	1.3657	20.40	0.244	45	F. W.	+++	26 yr.	C. S. L.
3425	2/26/23	7	0.2	30 m.	6.5186	1.2685	19.46	Trace	40	F. W.	Neg.	unknown	Tabes
3554	3/ 6/23	7	0.2	30 m.	5.7836	1.2179	21.05	0.25	44	M. W.	Neg.	24 yr.	Tabes
3135	1/25/23	23	0.2	30 m.	3.0147	0.6619	21.95	3.80	39	F. W.	++++	20 yr.	Tertiary syphilis
Interval—35 minutes (1 case)													
2864	1/10/23	11	0.25	35 m.	5.4673	1.5796	28.89	0.0633	38	M. W.	++++	1 yr.	Secondary syphilis
Interval—40 minutes (12 cases)													
3132	1/26/23	1	0.25	40 m.	6.3325	1.2798	20.21	0.384	24	F. B.	++++	?	Tertiary syphilis
2863	1/10/23	21	0.25	40 m.	5.3937	1.1951	22.15	0.167	25	M. W.	++	4 yr.	Tertiary syphilis
3106	1/29/23	16	0.2	40 m.	5.1853	1.0536	20.31	0.632	30	F. W.	++++	?	Tertiary syphilis
3098	1/29/23	0	0.2	40 m.	4.6267	0.8945	19.33	1.12	20	F. B.	++++	?	Tertiary syphilis
3137	1/26/23	2	0.25	40 m.	7.2797	1.3595	18.67	1.84	47	F. W.	++++	6 mo.	Secondary syphilis
2812	1/ 8/23	7	0.25	40 m.	5.5383	1.1969	21.61	0.042	32	M. B.	++++	?	Tertiary syphilis
83	1/31/21	1	0.15	40 m.	5.9996	1.3619	22.69	1.03	39	M. B.	++++	20 yr.	Tertiary syphilis
3136	1/20/23	4	0.2	40 m.	3.9371	0.8491	21.56	0.35	23	F. B.	++++	2 yr.	Tertiary syphilis
3100	1/29/23	47	0.2	40 m.	6.0235	1.2265	20.36	0.083	34	F. W.	++++	?	Tertiary syphilis
2817	1/ 8/23	2	0.25	40 m.	4.9939	0.8924	27.86	1.12	28	F. B.	++++	?	Tertiary syphilis
3147	1/24/23	1	0.25	40 m.	5.1071	1.0901	21.34	3.67	27	M. B.	++++	4 yr.	Tertiary syphilis
3101	1/29/23	0	0.2	40 m.	4.1503	0.8691	20.94	0.126	35	F. W.	++++	?	Tertiary syphilis

Interval—45 minutes (1 case)

2850	1/10/23	122	0.25	45 m.	5.2796	1.1398	21.59	0.0877	28	M.	W.	++++	7 yr.	Tertiary syphilis, Tabes

Interval—60 minutes (13 cases)

3129	1/26/23	15	0.2	60 m.	4.2126	0.7921	18.80	0.127	27	F.	W.	++++	5 mo.	Secondary syphilis
3123	1/24/23	75	0.25	60 m.	5.7161	1.3425	23.48	0.221	40	M.	W.	++++	20 yr.	Tertiary syphilis
84	1/31/21	1	0.15	60 m.	7.7206	1.6351	21.17	0.24	39	M.	B.	++++	20 yr.	Tertiary syphilis
2869	1/10/23	50	0.25	60 m.	4.7176	1.0283	21.79	0.985	30	M.	W.	++++	9 yr.	Tertiary syphilis, C. S. L.
2861	1/10/23	150	0.25	60 m.	4.8261	1.1360	23.53	0	28	M.	W.	Neg.	8 yr.	Optic atrophy
3128	1/24/23	7	0.25	60 m.	6.4478	1.2665	19.64	0.961	30	M.	B.	++++	3 yr.	Tertiary syphilis
3124	1/26/23	1	0.25	60 m.	5.1026	1.1790	23.15	0.085	37	M.	W.	++++	1 yr.	Tertiary syphilis
2853	1/10/23	7	0.25	60 m.	5.3788	1.2026	22.54	0.167	34	M.	W.	++++	1 yr.	Tertiary syphilis
3650	3/23/23	10	0.2	60 m.	5.9466	1.2537	21.08	0.956	26	F.	B.	++++	?	Tertiary syphilis
3659	3/23/23	4	0.2	60 m.	5.8215	1.1450	19.66	1.74	27	F.	B.	++++	4 mo.	Secondary syphilis
3652	3/23/23	15	0.25	60 m.	5.4398	1.0845	19.92	1.38	45	M.	W.	++++	?	Tertiary syphilis
3658	3/23/23	2	0.2	60 m.	6.8961	1.5346	22.25	0.652	20	M.	W.	++++	1 yr.	Secondary syphilis
3409	2/24/23	20	0.2	60 m.	5.8273	1.2188	20.91	3.33	45	F.	W.	+++	26 yr.	C. S. L.

Interval—24 hours (12 cases)

3008	1/16/23	2	0.2	24 hr.	4.4281	0.8834	19.98	Trace	57	M.	W.	++++	?	Tertiary syphilis
3006	1/16/23	16	0.25	24 hr.	4.1324	0.8553	20.71	0.058	47	M.	W.	++++	14 yr.	Neuro-syphilis
3213	1/30/23	50	0.2	24 hr.	5.2810	1.2271	23.23	2.43	43	F.	W.	++++	25 yr.	Tertiary syphilis
3007	1/15/23	20	0.25	24 hr.	3.4609	0.7896	19.98	0	37	M.	W.	++++	1½ yr.	Tertiary syphilis
3120	1/21/23	0	0.25	24 hr.	5.7620	1.1754	20.39	0.083	32	F.	W.	Neg.	14 yr.	Tertiary syphilis
3144	1/24/23	8	0.2	24 hr.	4.6555	1.0700	22.98	0.190	28	F.	B.	++++	?	Tertiary syphilis
3217	2/ 3/23	0	0.2	24 hr.	4.1970	1.8632	20.56	0.232	30	M.	W.	++++	?	Tertiary syphilis
3381	2/26/23	0	0.25	24 hr.	5.5459	1.1859	21.37	0.476	45	M.	W.	Neg.	12 yr.	Tertiary syphilis
3660	3/23/23	4	0.2	24 hr.	6.4486	1.2407	19.24	0.241	27	F.	B.	++++	4 mo.	Secondary syphilis
3661	3/23/23	32	0.25	24 hr.	9.2707	2.0993	22.64	0.238	51	M.	W.	+++	20 yr.	Tertiary syphilis
3653	3/23/23	15	0.25	24 hr.	5.5751	1.1272	20.21	0.708	45	M.	W.	++++	?	Tertiary syphilis
3649	3/23/23	0	0.2	24 hr.	5.9596	1.1740	19.69	0	40	M.	B.	++++	?	Tertiary syphilis

TABLE I—Continued

SERIAL NO.	DATE OF LAST INJECTION S. S.	NO. PREV. I. V. INJEC. SALV. NEO & S. S.	DOSE OF DRUG S. S.	TIME AFTER INJECTION	WT. OF SPECIMEN		PER CENT SOLIDS	AS. IN MGS. PER 100 GMS. DRIED SPEC.	AGE	SEX AND COLOR	WASS.	DURATION OF INFECTION	DIAGNOSIS AND REMARKS
					MOIST	DRY							
Interval—48 hours (13 cases)													
3140	1/24/23	30	0.2	48 hr.	5.4172	1.1765	21.71	0.700	25	F. W.	Neg.	3½ yr.	Tertiary syphilis
3142	1/24/23	30	0.25	48 hr.	3.9619	0.9290	23.46	1.08	31	M. W.	Neg.	3¼ yr.	Tertiary syphilis
2860	1/10/23	19	0.2	48 hr.	3.9960	0.8292	20.75	1.38	42	M. W.	++++	20 yr.	G. P. Optic atrophy
3243	1/31/23	16	0.2	48 hr.	4.7255	1.0580	22.39	0.566	23	M. W.	+++	2 yr.	C. S. L.
3215	2/ 2/23	1	0.2	48 hr.	5.3910	1.1419	21.18	0.438	27	F. W.	++++	6 mo.	Secondary syphilis
3121	1/26/23	0	0.25	48 hr.	5.6250	1.1273	20.04	0	32	F. W.	Neg.	14 yr.	Tertiary syphilis
3145	1/24/23	8	0.2	48 hr.	5.9433	1.3259	22.30	0.075	28	F. B.	++++	?	Tertiary syphilis
3684	3/26/23	2	0.25	48 hr.	6.2550	1.4790	23.64	0.067	25	M. W.	++++	4 mo.	Secondary syphilis
3436	2/26/23	17	0.25	48 hr.	5.9057	1.2060	20.41	0.082	23	M. W.	+++	4 yr.	Secondary syphilis
3438	2/26/23	0	0.25	48 hr.	5.4737	1.2533	22.91	0.080	45	M. W.	Neg.	12 yr.	Tertiary syphilis
3735	4/ 2/23	4	0.25	48 hr.	5.5749	1.0917	17.79	1.04	23	M. W.	++++	?	Secondary syphilis
3736	4/ 9/23	22	0.25	48 hr.	7.0149	1.4166	20.23	0.70	25	M. B.	Neg.	2 yr.	Tertiary syphilis
3737	4/ 2/23	13	0.25	48 hr.	5.3684	1.1532	21.47	0.26	41	M. W.	++++	?	C. S. L.
Interval—72 hours (21 cases)													
3240	2/ 2/23	1	0.2	72 hr.	6.9520	1.7340	24.98	0.589	30	M. W.	++++	10 yr.	Tertiary syphilis
3141	1/24/23	30	0.2	72 hr.	6.3597	1.2433	19.53	0.0803	25	F. W.	Neg.	3½ yr.	Tertiary syphilis
3143	1/24/23	30	0.25	72 hr.	5.8154	1.3241	22.78	0	31	M. W.	Neg.	3½ yr.	Tertiary syphilis
3496	3/ 5/23	10	0.25	72 hr.	5.8203	1.2765	21.93	0.937	25	M. W.	++++	4 yr.	Tertiary syphilis
3495	3/ 5/23	10	0.2	72 hr.	6.0425	1.3302	22.01	0.500	24	F. W.	++++	4 yr.	Tertiary syphilis
3497	3/ 5/23	8	0.25	72 hr.	6.4895	1.3801	21.66	0.072	25	M. B.	++	2½ yr.	Tertiary syphilis
3429	2/26/23	3	0.25	72 hr.	5.8314	1.3152	22.55	0	25	M. W.	++++	2 yr.	Tertiary syphilis
3261	2/ 7/23	9	0.2	72 hr.	6.1261	1.2926	21.10	0.800	15	M. W.	++++	1 yr.	Congenital syphilis

3212	1/29/23	30	0.25	72 hr.	5.0630	0.9564	18.88	0.833	25	F. W.	++++	10 yr.	Tertiary syphilis
3302	2/12/23	17	0.25	72 hr.	3.8884	0.7818	20.10	5.13	23	M. W.	+++	4 yr.	Secondary syphilis
3216	2/ 5/23	14	0.2	72 hr.	4.8210	0.9724	20.17	0.618	30	F. W.	++++	?	Tertiary syphilis
3439	2/26/23	0	0.25	72 hr.	5.8670	1.3091	22.19	1.53	45	M. W.	Neg.	12 yr.	Tertiary syphilis
3262	2/ 5/23	11	0.2	72 hr.	7.5540	1.3787	18.14	0.181	26	F. W.	++++	6 mo.	Secondary syphilis
3242	2/ 2/23	1	0.2	72 hr.	4.6840	0.9484	20.25	0.421	27	F. W.	++++	4 mo.	Secondary syphilis
3122	1/24/23	0	0.25	72 hr.	6.2947	1.2626	20.05	0.08	32	F. W.	Neg.	14 yr.	Tertiary syphilis
3540	2/ 9/23	0	0.25	72 hr.	6.4077	1.4009	21.86	0.071	43	M. W.	++	?	Tertiary syphilis
3264	2/ 9/23	0	0.25	72 hr.	7.5446	1.5571	20.62	0.320	40	M. B.	++++	2 mo.	Secondary syphilis
3498	3/ 5/23	4	0.2	72 hr.	6.4555	1.3447	20.52	1.13	35	F. W.	++++	?	Tertiary syphilis
3214	1/29/23	0	0.2	72 hr.	4.6236	0.9386	20.30	1.27	35	F. W.	++++	?	Tertiary syphilis
3146	1/24/23	8	0.2	72 hr.	4.7325	0.9910	20.94	0	28	F. B.	++++	?	Tertiary syphilis
3224	1/30/23	2	0.2	72 hr.	4.3630	0.8912	20.42	0	28	M. W.	Neg.	1 yr.	Secondary syphilis

Interval—96 hours (16 cases)

3687	3/23/23	6	0.25	96 hr.	5.2159	1.1708	22.44	0.341	27	M. W.	++++	9 yr.	Tertiary syphilis
3673	3/23/23	0	0.25	96 hr.	6.7565	1.3534	20.03	0.421	21	M. W.	++++	4 wk.	Secondary syphilis
3430	2/26/23	3	0.25	96 hr.	6.5763	1.4563	22.13	0.062	25	M. W.	++++	2 yr.	Tertiary syphilis
3686	3/23/23	8	0.2	96 hr.	5.5766	1.1756	21.08	0.085	30	F. W.	++++	4 mo.	Secondary syphilis
3667	3/23/23	5	0.25	96 hr.	6.0595	1.2115	19.99	0.082	39	M. W.	++++	5 yr.	Tertiary syphilis
3670	3/23/23	37	0.25	96 hr.	5.0242	1.0380	20.76	0.577	39	M. B.	++++	?	Tertiary syphilis
3668	2/23/23	2	0.25	96 hr.	6.4775	1.3525	20.88	0.073	30	M. W.	+++	10 yr.	Tertiary syphilis
3671	3/23/23	2	0.25	96 hr.	5.2810	1.0880	20.60	0.183	20	M. W.	+++	?	Tertiary syphilis
2964	1/12/23	2	0.2	96 hr.	4.5460	1.2036	26.48	0.664	26	F. W.	++++	2 mo.	Secondary syphilis
3669	3/23/23	23	0.2	96 hr.	5.9082	1.2307	20.82	0	45	M. W.	++++	15 yr.	Tertiary syphilis
2962	1/12/23	3	0.2	96 hr.	5.1760	0.9162	17.70	0.054	28	F. B.	++++	?	Tertiary syphilis
3666	3/23/23	2	0.25	96 hr.	6.8662	1.4833	21.60	1.01	20	M. W.	++++	1 yr.	Secondary syphilis
3189	1/30/23	2	0.2	96 hr.	6.9450	1.4512	20.88	0.133	28	M. W.	Neg.	1 yr.	Secondary syphilis
3063	1/18/23	6	0.2	96 hr.	6.3805	1.3168	20.63	0.454	37	M. W.	++++	12 yr.	Tabes
3416	2/22/23	3	0.2	96 hr.	5.5946	1.1831	21.12	1.41	35	M. W.	++++	12 yr.	Latent syphilis
3019	1/13/23	20	0.2	96 hr.	8.4756	1.6312	19.26	1.22	45	F. W.	++++	unknown	C. S. L.

TABLE I—Continued

SERIAL NO.	DATE OF LAST INJECTION S. S.	NO. PREV. I. V. INJEC. SALV. NEO & S. S.	DOSE OF DRUG S. S.	TIME AFTER INJECTION	WT. OF SPECIMEN		PER CENT SOLIDS	AS. IN MGS. PER 100 GMS. DRIED SPEC.	AGE	SEX AND COLOR	WASS.	DURATION OF INFECTION	DIAGNOSIS AND REMARKS
					MOIST	DRY							
Interval—120 hours (13 cases)													
3237		1	0.25	120 hr.	7.9200	1.8965	23.93	1.18	52	M. W.	++++	28 yr.	Tertiary syphilis
3241	1/31/23	0	0.2	120 hr.	4.8830	0.9447	19.35	0.319	28	F. B.	++++	4 mo.	Secondary syphilis
3539	3/ 5/23	10	0.25	120 hr.	5.3345	1.0682	20.02	2.80	43	M. W.	++	8 yr.	Tertiary syphilis
3685	3/22/23	7	0.25	120 hr.	5.4458	1.2083	22.18	0.165	37	M. B.	+	2 yr.	Tertiary syphilis
3236	1/31/23	0	0.2	120 hr.	7.1770	1.6779	23.37	2.90	25	F. W.	++++	6 wk.	Secondary syphilis
3688	2/23/23	2	0.25	120 hr.	5.5986	1.1444	20.44	0	30	M. W.	+++	10 yr.	Tertiary syphilis
3238	1/29/23	15	0.25	120 hr.	8.6200	2.2400	26.00	0.335	37	M. W.	Neg.	10 yr.	Tertiary syphilis
3689	3/23/23	2	0.25	120 hr.	4.5167	1.0642	23.56	0.093	20	M. W.	+++	?	Tertiary syphilis
3108	1/24/23	50	0.25	120 hr.	6.6065	1.4462	21.89	0.069	30	M. W.	++++	9 yr.	C. S. L.
3538	3/ 5/23	21	0.2	120 hr.	5.7478	1.2288	21.37	0.162	45	M. W.	Neg.	15 yr.	Tertiary syphilis
3672	3/21/23	5	0.25	120 hr.	8.4684	1.7208	20.32	0.174	24	M. W.	++++	?	Tertiary syphilis
3239	2/ 3/23	5	0.25	120 hr.	6.5178	1.2592	19.32	0.595	29	M. B.	++++	2 mo.	Secondary syphilis
3017	1/11/23	4	0.2	120 hr.	6.6525	1.3807	20.76	0.072	42	M. W.	Neg.	20 yr.	Optic atrophy
Interval—6 days (1 case)													
3265	1/31/23	22	0.15	6 da.	3.5363	0.7287	20.59	0.411	47	F. W.	Neg.	24 yr.	C. S. L.
Interval—1 week (5 cases)													
3286	2/ 1/23	19	0.2	1 wk.	6.2314	1.2197	19.58	0.491	40	F. W.	+++	18 yr.	C. S. L.
2978	1/ 6/23	18	0.2	1 wk.	6.2660	1.3067	20.85	0.0763	45	F. W.	+++	26 yr.	C. S. L.
2976	1/ 6/23	5	0.2	1 wk.	7.9213	1.7965	22.68	0.222	62	M. W.	++++	32 yr.	Tertiary syphilis
3424	2/19/23	6	0.2	1 wk.	5.7329	1.1166	19.48	2.23	40	F. W.	Neg.	unknown	Tabes
3060	1/18/23	18	0.2	1 wk.	5.5817	1.0426	18.68	0.048	40	F. W.	+++	11 yr.	C. S. L.

Interval—8 days (2 cases)

3159	1/18/23	0	0.2	8 da.	6.6381	1.4550	21.91	0.069	28	M. W.	Neg.	1 yr.	Secondary syphilis
3023	1/10/23	4	0.2	8 da.	7.1891	1.4243	20.09	0	37	M. W.	++++	12 yr.	Tabes

Interval—10 days (1 case)

3271	2/ 2/23	27	0.2	10 da.	3.4444	0.7497	21.75	0.333	42	M. W.	Neg.	23 yr.	Tabes

Interval—2 weeks (6 cases)

3157	1/13/23	6	0.2	2 wk.	5.9718	1.2560	21.03	0.396	50	M. W.	++++	unknown	Latent syphilis
3276	1/26/23	1	0.2	2 wk.	6.6690	1.3389	20.07	0.074	28	M. W.	Neg.	1 yr.	Secondary syphilis
3186	1/16/23	5	0.2	2 wk.	7.4599	1.5246	20.43	0.133	42	M. W.	Neg.	20 yr.	Optic atrophy
3184	1/16/23	21	0.15	2 wk.	3.7747	0.8221	21.77	1.22	47	F. W.	Neg.	24 yr.	C. S. L.
3220	1/20/23	16	0.2	2 wk.	4.4186	0.8765	19.83	0.454	31	F. W.	+++	15 yr.	Tertiary syphilis
3372	2/ 8/23	21	0.2	2 wk.	6.6342	1.2977	19.57	Trace	40	F. W.	+++	18 yr.	C. S. L.

Interval—3 weeks (5 cases)

3542	2/ 9/23	4	0.2	3 wk.	6.8750	1.4050	20.43	0.203	28	M. W.	Neg.	1 yr.	Secondary syphilis
3226	1/13/23	18	0.2	3 wk.	4.3942	0.8840	20.11	0.568	45	F. W.	+++	26 yr.	Tertiary syphilis
3408	2/ 3/23	19	0.2	3 wk.	7.1812	1.5247	21.25	0.065	45	F. W.	+++	26 yr.	Tertiary syphilis
3406	2/ 6/23	22	0.15	3 wk.	6.4290	1.3710	21.32	0.438	47	F. W	Neg.	24 yr.	C. S. L.
3269	1/20/23	22	0.2	3 wk.	4.6875	0.9849	21.00	0.305	51	M. W.	++++	15 yr.	Paresis

TABLE I—Continued

SERIAL NO.	DATE OF LAST INJECTION S. S.	NO. PREV. I. V. INJEC. SALV. NEO & S. S.	DOSE OF DRUG S. S.	TIME AFTER INJECTION	WT. OF SPECIMEN		PER CENT SOLIDS	AS. IN MGS. PER 100GMS. DRIED SPEC.	AGE	SEX AND COLOR	WASS.	DURATION OF INFECTION	DIAGNOSIS AND REMARKS
					MOIST	DRY							
Interval—1 month (3 cases)													
3710	2/23/23	17	0.2	1 mo.	4.8756	1.0124	20.74	0.098	50	M. W.	Neg.	14 mo.	Secondary syphilis
3015	12/15/22	0	0.2	1 mo.	6.0195	1.2657	21.02	0.400	19	M. W.	+	2 yr.	Neuro-syphilis
3064	12/21/22	7	0.2	1 mo.	9.2925	1.9138	20.58	0.053	48	M. W.	++++	23 yr.	Neuro-syphilis
Interval—5 weeks (1 case)													
3553	1/31/23	6	0.2	5 wk.	5.2685	1.0728	20.36	0.093	44	M. W.	Neg.	24 yr.	Tabes
Interval—6 weeks (1 case)													
3420	1/15/23	5	0.2	6 wk.	4.5356	0.9116	20.08	10.9	33	F. W.	Neg.	?	Tabes
Interval—7 weeks (1 case)													
2972	11/25/22	5	0.2	7 wk.	3.5733	1.1970	21.47	0.625	50	M. W.	++++	?	Latent syphilis

Interval—3 months (1 case)													
2898	10/12/22	10	0.25	3 mo.	7.3811	1.5292	20.71	0.261	25	M. B.	++	2 yr.	Tertiary syphilis
Interval—4 months (3 cases)													
2970	9/12/22	12	0.2	4 mo.	6.5054	1.4607	22.44	0	12	F. W.	++++	12 yr.	Congenital syphilis
3182	10/ 2/22	35	0.2	4 mo.	4.8500	0.9967	20.55	0.300	62	M. W.	Neg.		C. S. L.
3551	11/ 6/22	7	0.15	4 mo.	3.1128	0.6017	19.32	3.33	32	F. W.	++++	13 yr.	Tertiary syphilis
Interval—4½ months (1 case)													
2968	9/ /22	10	0.2	4½ mo.	5.0600	0.9667	19.10	0.31	28	F. W.	++++	?	Tertiary syphilis
Interval—8 months (1 case)													
3029	5/19/22	7	0.2	8 mo.	7.7700	1.6184	20.83	0.308	46	M. W.	+	25 yr.	Tabes

TABLE II.

ANALYSIS OF TABLE I BASED ON TIME INTERVALS; GIVING THE HIGHEST, THE LOWEST, AND THE AVERAGE VALUES OF ARSENIC FOR EACH GROUP

INTERVAL—IMMEDIATE

49 cases; 7 with negative, 42 with positive Wassermann reaction.

No. previous I. V. injections; 0.90.

Dose: 29 cases 0.2 gm.; 20 cases 0.25 gm. of silver salvarsan.

Smallest amount of arsenic: 0.089 mg. after 0.25 gm. and 1 previous injection; female, black, aged 27; tertiary syphilis.

Largest amount of arsenic: 10.0 mg. after 0.2 gm. and 6 previous injections; male, white, aged 45; tertiary syphilis.

Average amount of arsenic for this group: 2.62 mg.

INTERVAL—5 MINUTES

24 cases: 5 with negative, 19 with positive Wassermann reaction.

No. previous I. V. injections: 0.34.

Dose: 14 cases 0.2 gm.; 10 cases 0.25 gm. of silver-salvarsan.

Smallest amount of arsenic: 0.045 mg. after 0.25 gm. and 17 previous injections; female, white, aged 40; C. S. L.

Largest amount of arsenic: 3.44 mg. after 0.2 gm. and 1 previous injection; female, black, aged 29; tertiary syphilis.

Average amount of arsenic for this group: 1.24 mg.

INTERVAL—10 MINUTES

24 cases: 5 with negative; 19 with positive Wassermann reaction.

No. previous I. V. injections: 0-49.

Dose: 12 cases 0.2 gm.; 11 cases 0.25 gm.; 1 case 0.3 gm. of silver-salvarsan.

Smallest amount of arsenic: 0.0339 mg. after 0.2 gm., no previous injections; male, white, aged 40; tertiary syphilis.

Largest amount of arsenic: 3.40 mg. after 0.25 gm., 49 previous intravenous injections; male, white, aged 37; tertiary syphilis.

Average amount of arsenic for this group: 0.903 mg.

INTERVAL—15 MINUTES

22 cases: 3 with negative, 19 with positive Wassermann reaction.

No. previous I. V. injections: 0-48.

Dose: 7 cases 0.2 gm., 14 cases 0.25 gm., 1 case 0.15 gm. of silver-salvarsan.

Smallest amount of arsenic: 0 in two cases; one after 0.2 gm., 8 previous intravenous injections; male, white, aged 43; tertiary syphilis; the other after 0.2 gm. and 3 previous intravenous injections; male, white, aged 28; secondary syphilis.

Largest amount of arsenic: 1.90 mg. after 0.25 gm., 17 previous intravenous injections; male, white, aged 27; secondary syphilis.

Average amount of arsenic for this group: 0.61 mg.

TABLE II—Cont'd.

INTERVAL—20 MINUTES

19 cases: 6 with negative, 13 with positive Wassermann reaction.

No. Previous I. V. injections: 0.56.

Dose: 7 cases 0.2 gm., 12 cases 0.25 gm. of silver-salvarsan.

Smallest amount of arsenic: 0 after 0.25 gm., 6 previous intravenous injections; female, white, aged 39; paresis.

Largest amount of arsenic: 1.06 mg. after 0.2 gm., 5 previous intravenous injections; male, white, aged 42; optic atrophy.

Average amount of arsenic for this group: 0.48 mg.

INTERVAL—25 MINUTES

6 cases: 1 with negative, 5 with positive Wassermann reaction.

No. previous I. V. injections: 2-30.

Dose: 1 case 0.2 gm., 5 cases 0.25 gm. of silver salvarsan.

Smallest amount of arsenic: 0.046 mg. after 0.2 gm. and 2 previous I. V. injections; female, white, aged 25; tertiary syphilis.

Largest amount of arsenic: 1.755 mg. after 0.25 gm. and 4 previous I. V. injections; male, white, aged 37; tertiary syphilis.

Average amount of arsenic for this group: 0.74 mg.

INTERVAL—30 MINUTES

21 cases: 5 with negative, 16 with positive Wassermann reaction.

No. previous I. V. injections: 0-72.

Dose: 1 case 0.125 gm.; 10 cases 0.2 gm.; 9 cases 0.25 gm.; 1 case 0.3 gm.

Smallest amount of arsenic: 0 in three cases; one after 0.25 gm., and 60 previous I. V. injections; male, white, aged 30; tertiary syphilis; the second, after 0.2 gm. and 4 previous injections; female, white, aged 35; secondary syphilis; the third, after 0.2 gm. and 5 previous I.V. injections; male, white, aged 35; Neurosyphilis.

Largest amount of arsenic: 5.37 mg. after 0.2 gm. and 14 previous I.V. injections; female, white, aged 33; tertiary syphilis.

Average amount of arsenic for this group: 0.86 mg.

INTERVAL—35 MINUTES

1 case: Wassermann positive.

Amount of arsenic in this case: 0.0633 mg. after 0.25 gm. and 11 previous I.V. injections; male, white, aged 38; secondary syphilis.

INTERVAL—40 MINUTES

12 cases, all with positive Wassermann reaction.

Dose: 1 case 0.25 gm.; 5 cases 0.2 gm.; 6 cases 0.25 gm.

No. previous I.V. injections: 0-47.

Smallest amount of arsenic: 0.042 mg. after 0.25 gm. and 7 previous I. V. injections; male, black, aged 32; tertiary syphilis.

TABLE II—Cont'd.

Largest amount of arsenic: 3.67 mg. after 0.25 gm. and 1 previous injection; male, black, aged 27; tertiary syphilis.
Average amount of arsenic for this group: 0.88 mg.

INTERVAL—45 MINUTES

1 case: Wassermann positive.
Amount of arsenic: 0.0877 mg. after 0.25 gm. and 122 previous I. V. injections; male, white, aged 28; tertiary syphilis.

INTERVAL—60 MINUTES

13 cases: 1 with negative, 12 with positive Wassermann reaction.
Dose: 1 case, 0.15 gm.; 5 cases, 0.2 gm.; 7 cases, 0.25 gm.
No. previous I. V. injections: 1-150.
Smallest amount of arsenic: 0 after 0.25 gm. and 150 previous I. V. injections; male, white, aged 28; optic atrophy.
Largest amount of arsenic: 3.33 mg. after 0.2 gm. and 20 previous I. V. injections; female, white, aged 45; Neurosyphilis.
Average amount of arsenic for this group: 0.83 mg.

INTERVAL—24 HOURS

12 cases: 2 with negative and 10 with positive Wassermann reaction.
Dose: 6 cases 0.2 gm., 6 cases 0.25 gm.
No. previous I. V. injections: 0-50.
Smallest amount of arsenic: 0 in two cases; one after 0.25 gm. and 20 previous injections; male, white, aged 37, tertiary syphilis; the other, after 0.2 gm. and 0 previous injections; male, black, aged 40; tertiary syphilis.
Largest amount of arsenic: 2.43 mg. after 0.2 gm. and 50 previous injections; female, white, aged 43; tertiary syphilis.
Average amount of arsenic for this group: 0.39 mg.

INTERVAL—48 HOURS

13 cases: 5 with negative and 8 with positive Wassermann reaction.
No. previous I. V. injections: 0-30.
Dose of Drug: 5 cases 0.2 gm.; 8 cases 0.25 gm.
Smallest amount of arsenic: 0 after 0.25 gm. and 0 previous injection; female, white, aged 32; tertiary syphilis.
Largest amount of arsenic: 1.38 mg. after 0.2 gm. and 19 previous injections; male, white, aged 42, G. P.; optic atrophy.
Average amount of arsenic for this group: 0.50 mg.

INTERVAL—72 HOURS

21 cases: 5 with negative and 16 with positive Wassermann reaction.
No. previous I. V. injections: 0-30.
Dose: 11 cases 0.2 gm.; 10 cases 0.25 gm.

TABLE II—Cont'd.

Smallest amount of arsenic: 0 in 4 cases; diagnoses in these cases are as follows: 3 with tertiary syphilis, and one with secondary syphilis.

Largest amount of arsenic: 5.13 mg. after 0.25 gm. and 17 previous I V. injections; male, white, aged 23; secondary syphilis.

Average amount of arsenic for this group: 0.69 mg.

INTERVAL—96 HOURS

16 cases: 1 negative, 15 with positive Wassermann reaction.

No. previous injections: 0-37.

Dose: 8 cases 0.2 gm., 8 cases 0.25 gm.

Smallest amount of arsenic: 0 after 0.2 gm. and 23 previous I. V. injections; male, white, aged 45; tertiary syphilis.

Largest amount of arsenic: 1.41 mg. after 0.2 gm. and 3 previous injections; male, white, aged 35; latent syphilis.

Average amount of arsenic: 0.42 mg.

INTERVAL—120 HOURS

13 cases: 3 with negative and 10 with positive Wassermann reaction.

No. previous I. V. injections: 0-50.

Dose: 4 cases 0.2 gm.; 9 cases 0.25 gm.

Smallest amount of arsenic: 0 after 0.25 and 0 previous injections; male, white, aged 30; tertiary syphilis.

Largest amount of arsenic: 2.9 mg. after 0.2 gm and 0 previous injections; female, white, aged 25; secondary syphilis.

Average amount of arsenic: 0.68 mg.

INTERVAL—6 DAYS

1 case: with negative Wassermann reaction.

Amount of arsenic for this case: 0.411 mg. after 0.15 gm. and 22 previous injections; female, white, aged 47; Neurosyphilis.

INTERVAL—1 WEEK

5 cases: 1 with negative and 4 with positive Wassermann reaction.

No. previous injections: 5-19.

Dose: 0.2 gm. in all cases.

Smallest amount of arsenic: 0.048 mg. after 0.2 gm. and 18 previous injections; female, white, aged 40; Neurosyphilis.

Largest amount of arsenic: 2.23 mg. after 0.2 gm. and 6 previous injections; female, white, aged 40; tabes.

Average amount of arsenic: 0.61 mg.

TABLE II—Cont'd.

INTERVAL 8 DAYS

2 cases: 1 negative; one with positive Wassermann reaction.

Smaller amount of arsenic: 0 after 0.2 gm. and 4 previous injections; male, white, aged 37; tabes.

Larger amount of arsenic: 0.069 mg. after 0.2 gm. and 0 previous injections; male, white, aged 28; secondary syphilis.

Average amount of arsenic for these two cases: 0.0345 mg.

INTERVAL—10 DAYS

1 case with negative Wassermann reaction.

Amount of arsenic: 0.333 mg. after 0.2 gm. and 27 previous injections; male, white, aged 42; tabes.

INTERVAL—2 WEEKS

6 cases: 3 with negative, 3 with positive Wassermann reaction.

No. previous injections: 1-21.

Dose: 1 case 0.15 gm.; 5 cases 0.2 gm.

Smallest amount of arsenic: trace after 0.2 gm. and 21 previous injections; female, white, aged 40; Neurosyphilis.

Largest amount of arsenic; 1.22 mg. after 0.15 gm. and 21 previous injections; female, white, aged 47; Neurosyphilis.

Average amount of arsenic for this group: 0.38 mg.

INTERVAL—3 WEEKS

5 cases: 2 with negative, 3 with positive Wassermann reaction.

No. previous injections: 4-22.

Dose: 1 case 0.15 gm., 4 cases, 0.2 gm.

Smallest amount of arsenic: 0.065 mg. after 0.2 gm. and 19 previous injections; female, white, aged 45; tertiary syphilis.

Largest amount of arsenic: 0.568 mg. after 0.2 gm. and 18 previous injections; female, white, aged 45; tertiary syphilis.

N. B.—The specimens in this interval containing the smallest and largest amounts of arsenic are from the same patient.

Average amount of arsenic for this group: 0.31 mg.

INTERVAL—1 MONTH

3 cases; 1 with negative. 2 with positive Wassermann reaction.

No. previous injections; 0-17.

Dose; 0.2 gm.

Smallest amount of arsenic; 0.053 mg. after 0.2 gm. and 7 previous injections, male, white, aged 48; neurosyphilis.

TABLE II—Cont'd.

Largest amount of arsenic; 0.4 mg. after 0.2 gm. and 0 previous injections, male, white, aged 19; neurosyphilis.

Average amount of arsenic; 0.18 mg.

INTERVAL—5 WEEKS

1 case with negative Wassermann reaction.

Amount of arsenic; 0.093 mg. after 0.2 gm. and 6 previous injections; male, white, aged 44, tabes.

INTERVAL—6 WEEKS

One case with negative Wassermann reaction.

Amount of arsenic: 10.9 mg. after 0.2 gm. and 5 previous injections, female, white, aged 33, tabes.

INTERVAL—7 WEEKS

One case with positive Wassermann reaction.

Amount of arsenic: 0.625 mg. after 0.2 gm. and 5 previous injections, male, white, aged 50, latent syphilis.

INTERVAL—3 MONTHS

One case with positive Wassermann reaction.

Amount of Arsenic: 0.261 mg. after 0.25 gm. and 10 previous injections, male, black, aged 25, tertiary syphilis.

INTERVAL—4 MONTHS

3 cases; 1 with negative; 2 with positive Wassermann reaction.

No. previous I.V. injections: 7-35.

Dose of Drug: 0:15 gm. in 1 case; 0.2 gm. in 2 cases.

Smallest amount of arsenic: 0 after 0.2 gm. and 12 previous injections, female, white, aged 12, congenital syphilis.

Largest amount of arsenic: 3.33 mg. after 0.15 gm. and 7 previous injections, female, white, aged 32, tertiary syphilis.

Average amount of arsenic: 1.21 mg.

INTERVAL—4½ MONTHS

One case with positive Wassermann reaction.

Amount of arsenic: 0.31 mg. after 0.2 gm. and 10 previous injections, female, white, aged 28, tertiary syphilis.

INTERVAL—8 MONTHS

One case with positive Wassermann reaction.

Amount of Arsenic: 0.308 mg. after 0.2 gm. and 7 previous injections, male, white, aged 36, tabes.

TABLE III

CLASSIFIED ACCORDING TO THE QUANTITY OF ARSENIC FOUND IN THE BLOOD, TIME INTERVAL, AND STAGE OF THE DISEASE

STAGE OF DISEASE	TIME INTERVAL	AMOUNT OF ARSENIC PER 100 GMS. DRIED SPECIMEN
	No Arsenic	
Secondary Syphilis	15 Minutes	
	30 “	
	72 Hours	
Tertiary Syphilis		
1. Without involvement of the central nervous system	15 Minutes	
	30 “	
	24 Hours	
	24 “	
	48 “	
	72 “	
	72 “	
	72 “	
	96 “	
	120 “	
With involvement of the central nervous system	20 Minutes	
	30 “	
	60 “	
	8 Days	
Congenital Syphilis	4 Months	
	Indeterminate Amounts of Arsenic	
Tertiary Syphilis	24 Hours	
2. Without involvement of the central nervous system		
With involvement of the central nervous system	30 Minutes	
	2 Weeks	
	0.0339 *mg. to* 5.0 *mg. arsenic per* 100 *gm. dried specimen*	
Primary Syphilis	30 Minutes	1.00 mg.
	30 “	1.24 “
Secondary Syphilis	0 “	2.32 “
	0 “	0.942 “
	0 “	0.310 “
	0 “	0.878 “
	0 “	0.588 “
	0 “	0.308 “
	0 “	1.699 “
	0 “	0.869 “
	5 “	1.70 “
	5 “	0.062 “
	10 “	0.132 “
	10 “	2.08 “
	10 “	0.4444 “
	10 “	1.11 “

TABLE III—Cont'd.

STAGE OF DISEASE	TIME INTERVAL	AMOUNT OF ARSENIC PER 100 GMS. DRIED SPECIMEN
0.0339 *mg. to* 5.0 *mg. arsenic per* 100 *gm. dried specimen* (continued)		
	10 “	0.857 “
	10 “	0.182 “
	10 “	1.09 “
	10 “	1.76 “
	15 “	0.1772 “
	15 “	0.390 “
	15 “	0.480 “
	15 “	0.84 “
	15 “	1.90 “
	20 “	0.082 “
	20 “	0.381 “
	20 “	0.798 “
	25 “	0.187 “
	30 “	0.225 “
	30 “	1.70 “
	35 “	0.0633 “
	40 “	1.84 “
	60 “	0.127 “
	60 “	1.74 “
	60 “	0.652 “
	24 Hours	0.241 “
	48 “	0.438 “
	48 “	0.067 “
	48 “	0.082 “
	48 “	1.04 “
	72 “	0.181 “
	72 “	0.421 “
	72 “	0.320 “
	96 “	0.421 “
	96 “	0.085 “
	96 “	0.664 “
	96 “	1.01 “
	96 “	0.133 “
	120 “	0.319 “
	120 “	2.90 “
	120 “	0.595 “
	8 Days	0.0690 “
	2 Weeks	0.074 “
	3 Weeks	0.203 “
	1 Month	0.098 “
Latent syphilis	0 Minutes	0.219 “
	0 “	0.496 “
	5 “	1.45 “
	10 “	2.15 “
	96 Hours	1.41 “
	2 Weeks	0.396 “
	7 “	0.625 “

TABLE III—Cont'd.

STAGE OF DISEASE	TIME INTERVAL	AMOUNT OF ARSENIC PER 100 GM. DRIED SPECIMEN
0.0339 *mg. to* 5.0 *mg. arsenic per* 100 *gm. dried specimen* (continued)		
Tertiary syphilis 1. Without involvement of the central nervous system	0 Minutes	0.432 "
	0 "	0.089 "
	0 "	0.816 "
	0 "	1.15 "
	0 "	0.337 "
	0 "	0.593 "
	0 "	1.82 "
	0 "	0.501 "
	0 "	4.51 "
	0 "	2.73 "
	0 "	4.20 "
	0 "	1.53 "
	0 "	4.55 "
	0 "	2.56 "
	0 "	1.34 "
	0 "	2.39 "
	0 "	0.314 "
	0 "	2.71 "
	0 "	1.86 "
	0 "	0.201 "
	0 "	1.87 "
	0 "	1.80 "
	5 "	0.326 "
	5 "	0.454 "
	5 "	0.317 "
	5 "	2.62 "
	5 "	3.44 "
	5 "	2.22 "
	5 "	1.71 "
	5 "	0.277 "
	5 "	1.81 "
	5 "	3.20 "
	5 "	3.36 "
	5 "	2.08 "
	5 "	0.074 "
	10 "	3.40 "
	10 "	0.69 "
	10 "	0.0339 "
	10 "	0.41 "
	10 "	0.858 "
	10 "	0.13 "
	10 "	0.33 "
	10 "	1.56 "
	10 "	1.27 "
	15 "	0.201 "
	15 "	0.949 "
	15 "	1.08 "
	15 "	0.931 "
	15 "	0.220 "
	15 "	1.12 "
	15 "	1.11 "

TABLE III—Cont'd.

STAGE OF DISEASE	TIME INTERVAL	AMOUNT OF ARSENIC PER 100 GM. DRIED SPECIMEN
0.0339 *mg. to* 5.0 *mg. arsenic per* 100 *gm. dried specimen* (continued)		
	15 “	0.590 “
	15 “	0.865 “
	15 “	0.241 “
	15 “	0.164 “
	15 “	0.395 “
	20 “	0.525 “
	20 “	0.407 “
	20 “	0.184 “
	20 “	0.317 “
	20 “	0.168 “
	20 “	1.008 “
	25 “	1.39 “
	25 “	0.222 “
	25 “	0.046 “
	25 “	1.755 “
	30 “	0.222 “
	30 “	0.73 “
	30 “	1.12 “
	30 “	0.0402 “
	30 “	0.452 “
	30 “	1.22 “
	30 “	0.34 “
	30 “	3.80 “
	40 “	0.384 “
	40 “	0.167 “
	40 “	0.632 “
	40 “	1.12 “
	40 “	0.042 “
	40 “	1.03 “
	40 “	0.35 “
	40 “	0.083 “
	40 “	1.12 “
	40 “	3.67 “
	40 “	0.126 “
	45 “	0.0877 “
	60 “	0.221 “
	60 “	0.24 “
	60 “	0.961 “
	60 “	0.085 “
	60 “	0.167 “
	60 “	0.956 “
	60 “	1.38 “
	24 Hours	2.43 “
	24 “	0.083 “
	24 “	0.190 “
	24 “	0.232 “
	24 “	0.476 “
	24 “	0.238 “
	24 “	0.708 “
	48 “	0.700 “
	48 “	1.08 “

TABLE III—Cont'd.

STAGE OF DISEASE	TIME INTERVAL	AMOUNT OF ARSENIC PER 100 GM. DRIED SPECIMEN
0.0339 *mg. to* 5.0 *mg. arsenic per* 100 *gm. dried specimen* (continued)		
	48 "	0.075 "
	48 "	0.080 "
	48 "	0.70 "
	72 "	0.589 "
	72 "	0.0803 "
	72 "	0.937 "
	72 "	0.500 "
	72 "	0.072 "
	72 "	0.833 "
	72 "	0.618 "
	72 "	1.53 "
	72 "	0.08 "
	72 "	0.071 "
	72 "	1.13 "
	72 "	1.27 "
	96 "	0.341 "
	96 "	0.062 "
	96 "	0.082 "
	96 "	0.577 "
	96 "	0.073 "
	96 "	0.183 "
	96 "	0.054 "
	120 "	1.18 "
	120 "	2.80 "
	120 "	0.165 "
	120 "	0.335 "
	120 "	0.093 "
	120 "	0.162 "
	120 "	0.174 "
	1 Week	0.222 "
	2 Weeks	0.454 "
	3 "	0.568 "
	3 "	0.065 "
	3 Months	0.261 "
	4 "	3.33 "
	4½ "	0.31 "
Tertiary syphilis	0 Minutes	0.268 "
2. With involvement of the central nervous system	0 "	0.565 "
	0 "	0.835 "
	0 "	2.55 "
	0 "	0.926 "
	0 "	4.11 "
	0 "	2.05 "
	5 "	0.045 "
	5 "	0.611 "
	5 "	1.52 "
	5 "	0.571 "
	5 "	0.222 "
	5 "	0.259 "
	5 "	0.877 "

TABLE III—Cont'd.

STAGE OF DISEASE	TIME INTERVAL	AMOUNT OF ARSENIC PER 100 GM. DRIED SPECIMEN
0.0339 *mg. to* 5.0 *mg. arsenic per* 100 *gm. dried specimen* (continued)		
	10 “	0.184 “
	10 “	0.161 “
	10 “	0.245 “
	10 “	1.31 “
	15 “	0.216 “
	15 “	0.050 “
	15 “	0.993 “
	20 “	0.510 “
	20 “	0.372 “
	20 “	0.946 “
	20 “	0.781 “
	20 “	1.06 “
	20 “	0.47 “
	20 “	0.438 “
	20 “	0.136 “
	20 “	0.408 “
	25 “	0.8400 “
	30 “	0.908 “
	30 “	0.165 “
	30 “	0.244 “
	30 “	0.25 “
	60 “	0.985 “
	60 “	3.33 “
	24 Hours	0.058 “
	48 “	1.38 “
	48 “	0.566 “
	48 “	0.26 “
	96 “	0.454 “
	96 “	1.22 “
	120 “	0.069 “
	120 “	0.072 “
	6 Days	0.411 “
	1 Week	0.491 “
	1 “	0.0763 “
	1 “	2.23 “
	1 “	0.048 “
	2 Weeks	0.133 “
	2 “	1.22 “
	3 “	0.438 “
	3 “	0.305 “
	1 Month	0.400 “
	1 “	0.053 “
	5 Weeks	0.093 “
	4 Months	0.300 “
	8 Months	0.308 “
Congenital syphilis	10 Minutes	0.143 “
	72 Hours	0.800 “
Non-syphilitic Cases	0 Minutes	0.419 “
	5 “	1.50 “

TABLE III—Cont'd.

STAGE OF DISEASE	TIME INTERVAL	AMOUNT OF ARSENIC PER 100 GM. DRIED SPECIMEN
5.0 mg. to 10.9 mg. arsenic per 100 gm. dried specimen		
Secondary syphilis	0 Minutes	7.35 "
	0 "	6.60 "
	72 Hours	5.13 "
Tertiary syphilis 1. Without involvement of the central nervous system	0 Minutes	7.80 "
	0 "	8.82 "
	0 "	5.60 "
	0 "	10.00 "
	0 "	7.27 "
	0 "	9.30 "
	5 "	5.37 "
Tertiary syphilis 2. With involvement of the central nervous system	6 Weeks	10.9 "
Non-syphilitic Case	0 Minutes	7.15 "

TABLE IV

A SUMMARY OF THE AVERAGE AMOUNT OF ARSENIC AND AVERAGE TOTAL SOLIDS BASED ON TIME INTERVALS WITH NUMBER OF CASES IN EACH GROUP

TIME	NO. OF CASES	AVERAGE AS.	AVERAGE TOTAL SOLIDS
0+	49	2.62 gm.	19.77
5 min.	24	1.24 "	20.47
10 min.	24	0.903 "	20.47
15 min.	22	0.61 "	21.74
20 min.	19	0.48 "	21.59
25 min.	6	0.74 "	20.94
30 min.	21	0.86 "	21.52
40 min.	12	0.88 "	21.33
60 min.	13	0.83 "	21.38
24 hrs.	12	0.39 "	20.91
48 hrs.	13	0.50 "	21.40
72 hrs.	21	0.69 "	20.99
96 hrs.	16	0.42 "	21.03
120 hrs.	13	0.68 "	21.73
1 week	5	0.61 "	20.20
2 weeks	6	0.38 "	20.35
3 weeks	5	0.31 "	21.40

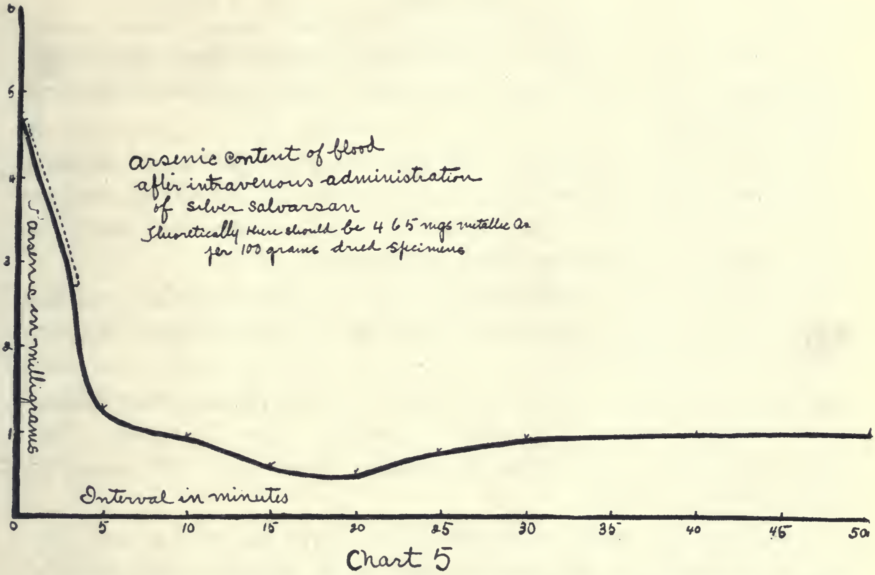

Chart 5.—Graphically shows the arsenic present in the blood stream at varying intervals as illustrated in column III of Table IV. Milligrams of metallic arsenic in 100 grams of dried specimen are plotted against intervals in minutes. The dotted line shows the theoretical fall in arsenic content of the blood during the injection interval.

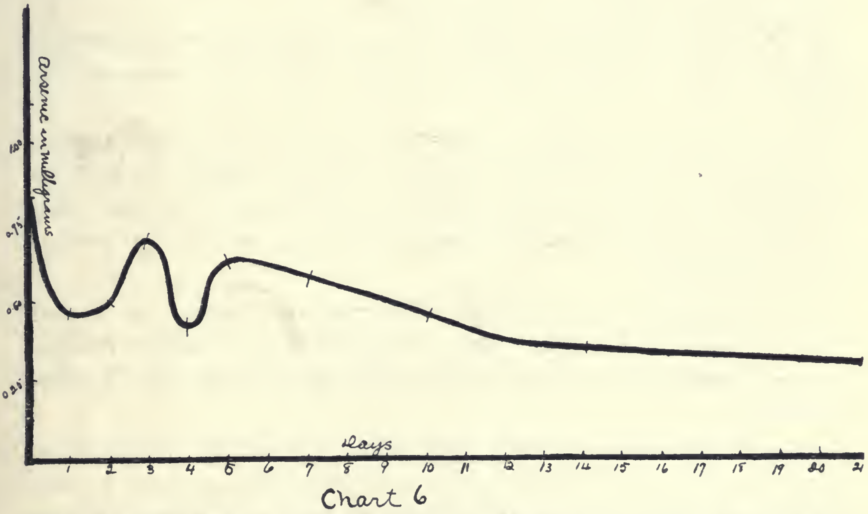

Chart 6.—Milligrams of metallic arsenic in 100 grams of dried specimen are plotted against intervals in days.

SUMMARY

1. Analyses of the blood for its arsenic content after intravenous injections of silver salvarsan were made in 299 specimens obtained from 214 patients.

2. Table I gives a complete classification of the patients in regard to age, sex, previous treatment and stage of the disease in correlation with the specimen used and the arsenic content expressed in milligrams per 100 grams of dried specimen.

3. Analysis of blood taken immediately after the completion of the injection shows that 56.4 per cent of the arsenic injected localizes outside of the blood stream.

4. The maximum quantity of arsenic in the blood stream, based upon average values, is found immediately after injection. The value expressed in milligrams of metallic arsenic per 100 grams of dried specimen is 2.62.

5. Observations made at intervals from five minutes to one day show that there is a gradual lowering of the arsenic equilibrium in the blood, based on average values.

6. Observations made after a period of one day show first a marked increase in the arsenic content and then a gradual diminution at later intervals, based on average values.

7. The above results are taken from the averages of all types of patients in the various stages of syphilis and a few non-syphilitic cases.

8. Abnormal values, both high and low, for any given interval (partition coefficient) are met with in certain individuals with an arsenic idiosyncrasy or predisposition to intoxication by the drug.

9. Rapid localization of the arsenic may be a warning for certain later intoxications.

10. Two groups of individuals, who may be classified as "short period" and "long period" show irregularity of arsenical fluctuations in excretion and retention after intravenous injections of silver salvarsan.

11. Examination of Table I shows that the rate of partition between the blood and tissues varies with individual patients so that attempts to bring about arsenic saturation in an individual demand careful control of the patient.

12. Variations of arsenic content and possible variations of therapeutic activity were eliminated by using the same control number of the drug throughout this investigation.

13. Table IV gives the average amount of arsenic in milligrams per 100 grams of dried specimen at intervals from immediately after injection to a period of three weeks. The average total solids for each interval and the number of cases examined are recorded in adjoining columns.

14. The study of other data tabulated in this paper and the problems suggested in article I are now complete. Our conclusions are reserved until the entire material is presented, thereby enabling a more satisfactory decision as to the results obtained from nearly 5,000 determinations.

CHANCRE IN THE AXILLA

By Douglass W. Montgomery, M.D., and George D. Culver, M.D.,
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Received for publication, May 8, 1923

CHANCRE of course may occur in any part of the body where inoculated, but it is rarely found in the axilla.

In countries where the people are cleanly in their habits, and not overcrowded in their habitations, extragenital chancre is not frequent and constitutes only about eight per cent of the entire number. On the other hand, in countries where the people are inveterately dirty, and afflicted with an extreme corporeal sociability, as in Russia, the incidence of extragenital chancre can rise even to ninety-two per cent.[1]

The greater cleanliness of the medical profession during the past years has had a marked effect on the occurrence of extragenital chancre. For instance, in looking over the medical reports in the sixth decade of the last century, before the advent of aseptics and antiseptics, one is struck by the frequency of chancre of the Eustachian tube transmitted by the catheter, and chancre transmitted in vaccination, both of which must now be very rare.

After the genital organs, by far the greater number of chancres occur about the head, then the breasts and nipples, then the fingers and hands. In other regions chancre is very rare indeed. In our practice there has been one of the foot and one of the axilla, two exceedingly unusual situations.

Contagion may take place by the most diverse intermediaries:

1. Through dirty surgical instruments, an occurrence now rare;
2. Through borrowed garments, such as trousers soiled by their previous wearers; a reasonable enough way of transmission considering the carelessness in bandaging chancres, or not bandaging them at all. We shall see that our patient probably acquired her infection through a garment she had lent a neighbor.
3. Through bed linen and coverlets;
4. Through bath linen, combs and gloves;
5. In washing the linen of syphilitics;

A laundress is reported to have acquired a chancre of the sole in

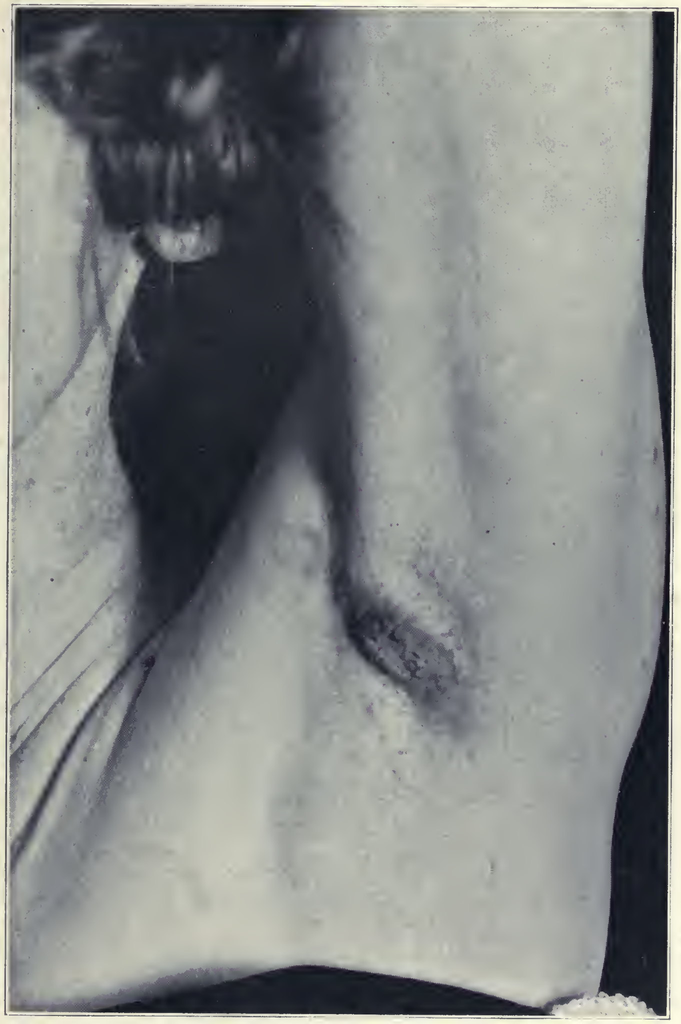

Fig. 1.—Chancre of axilla. Attention may be called to the anfractuous, impetiginous surface. The dark color indicates the deep red congestion of the lesion, which resembled strikingly a tuberculous ulcer.

washing the linen of prostitutes by tramping it with the bare feet in a tub of water.[2]

6. By the always discredited but not altogether improbable water closet.

On Jan. 16, 1920, I was called to see an unmarried woman, twenty-seven years of age, who had an extensive papulopustular eruption which had recently appeared. It was so markedly pustular as to have given rise, in the mind of the physician who recommended her to me, that she might have smallpox. She was so ill as to be confined to her bed.

Although the eruption was unusually pustular, and also unusually uniform for syphilis (for instance, there was no roseola), yet its general appearance gave an undeniably luetic impression. There were no mucous patches. Then began the hunt for the chancre, and for other concomitant luetic symptoms. She said that more than a month previously, on Dec. 10, she had noticed a pimple in the left axilla. This grew worse and was lanced Dec. 17, and in all was lanced three times. On Dec. 26, she got a chill with violent headache, and ran a temperature of 101°-102° for twelve days. I saw the patient first on Jan. 16, and the eruption had but recently appeared.

The chancre was a large, deep red, infiltrated, but not indurated lesion, covered with a heavy impetiginous crust, and situated high up on the chest wall of the left axilla. The incriminating, large, oval, lymphatic nodule was found just above it. The Wassermann reaction was positive.

For a long time the patient was very ill, but the eruption responded well to the treatment. The chancre site remained for a long time as a deep red spot with some thickening.

Chancre on hairy surfaces acts in a peculiar way, and Finger gives one of the best descriptions of its course.[3] It begins as a pustule at the point of emergence of a hair, and goes on to the formation of an impetiginous lesion with a crumbly, dark crust and with some thickening, but no characteristic induration at its base. In other words, it does not give any definite indications of its real nature. It is unusually persistent, and its base becomes deep red. These two features might put one on the alert, but it is too much to expect one to be so much on the alert in a situation like the axilla where pyogenic lesions are so frequent and chancre is so rare. When I arrived I had the eruption to guide me, and it was an instance of the old saying, "Happy is the man who is called last in a case."

In searching for the source of the infection the patient became as enthusiastic as ourselves. In one instance in the literature the infection was traced to the employment of a dirty scalpel in opening an abscess.[4] Although this lesion had been lanced three times, circumstances precluded this mode of transmission. We then thought of its transmission by shaving the axilla, so frequently practiced now, but after careful consideration this was also dismissed. The possibility of the virus being communicated by unnatural sexual practices was also found to be too remote to be entertained seriously. Then the patient recalled that a woman of rather questionable morals, and who was ill and suffered from an eruption, lived in the same apartment building. This woman, because of her illness and dejection, excited the patient's pity and some time before the appearance of the lesion in the axilla, she had lent her a wrapper, which on being returned, she herself wore. The present mode of dress would bring this wrapper in close approximation with the axilla, and furthermore, early cutaneous luetic lesions are frequent about the shoulders, and their secretions could easily soil the garment in this situation. A pimple in the axilla would furnish the portal of entrance for the virus.

REFERENCES

[1] In some provinces of Russia the incidence of extragenital chancres reaches from seventy-four to ninety-two per cent. Die Geschlechtskrankheiten, von E. Finger, 1908, S. 35.

[2] Syphilis, by Professor Dr. A. Buschke, Lehrbuch der Haut und Geschlechtskrankheiten, Herausgegeben von E. Riecke, 1914, S. 648.

[3] Die Geschlechtskrankheiten, von E. Finger, Loc. cit.

[4] Köbner relates a case in which he saw a chancre supervene after incising an abscess in the axilla. Quoted by Edmond Fournier, Traité de la Syphilis, 1903, page 163.

CHANCRE OF THE LIP*

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(Received for publication, April 19, 1923)

THE most frequent location for extragenital chancre is the mouth, and by far the greatest number on the lips. Kissing is probably the most common way of infection, but intermediate objects have been claimed by a number of patients thought to be reliable. Very often the innocent boy or girl can see no harm in permitting the familiarity of a caress on the lips since the knowledge of contagion from this source is not so generally known or feared as more intimate relations. One need but mention the famous epidemic of lip chancres from a kissing game to recall this. Bulkley, Scheube, Porter and others have collected instances of chancres of the lips. The incidence of lip chancre acquired by perversions is thought to be extremely low. For evident reasons the number of women with lip chancre is larger than of men. Vedder's table should not be overlooked and is based on Scheube's work:

Buccal Contact

Kissing	192	
Instruments used in certain callings, glass blowers, musicians, chemists	37	
Smokers articles	28	
Drinking glasses	26	
Eating utensils	22	
Toothpicks	5	
Artificial feeding of children	10	
	320	22.07 per cent

The list is a good sermon for the avoidance of promiscuous kissing. The chancre has an incubation time of ten days to one month. The primary sore appears at the site of inoculation. The location of the lesion has much to do with its clinical appearance. The primary sore of syphilis is usually single, occasionally multiple.

The enlarged lymphatic glands are usually found from one to two weeks after the appearance of the initial sore.

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*Illustrated by photographs from the Collections of Parounagian and Goodman.

Although there has been no unanimity in reports as to whether the upper or lower lip is more frequently affected, our experience has been that the lower lip is affected twice as often as the upper.

The chancre of the lip as may be learned from a review of the photographs accompanying this contribution cannot be standardized. A description that would fit all chancres cannot be given. Ordinarily as described in the text books, the chancre is held to be round or oval, and generally covered with a scab or crust which is difficult to remove, and leaves a raw, easily bleeding surface beneath it. Owing to the looseness of the tissues of the lips the associated edema is well marked. The ulceration varies in size from that of split pea to a five cent piece. The tendency for chancres of the lip is to hypertrophy. In the early stages the induration at the base is not so well marked, and the lesion may be diagnosed as herpes, impetigo, or other septic infection. As the sore does not react to local applications the induration rapidly shows itself and the diagnosis soon becomes obvious.

CASE HISTORIES

One of our most interesting cases, and one replete with warnings and lessons, was that of Miss R. B., aged nineteen years. About two weeks after she had permitted a boy friend to kiss her, a small pimple was noticed on the upper lip. She visited her physician who made a clinical examination and prescribed some local application. The lesion persisted and indeed became larger, so that a consultation with another physician followed. The result was that a diagnosis of probable tuberculosis was reached. The patient complained of pains, despite the medication given, and a second consultant was called. A conclusion of rheumatism, and skin lesions accompanying the same was reached. No hint of the possible syphilitic nature of the lesion was suspected, even when the glands under the chin began to enlarge, which they did about three and one-half weeks after the first appearance of the sore. About six weeks after the sore was noticed, there was a general eruption of the body, and at this time a Wassermann was reported 4-plus. She came to us then with a large, ulcerated lesion of the upper lip, a little to the left of the midline, with much edema, an enlargement of the glands under the chin, a secondary papular syphilide, and mucous patches of the throat. She was placed on treatment immediately, and in view of the character of the lesion, the general run down condition of the patient, and the fact that she was a source of contagion to her immediate family, hospitalization was recommended. After a course of intravenous injections, the Wassermann became negative, and has persisted negative for over a year. She had a course of intramuscular mercury salicylate injections, once a week for fifteen weeks after the cessation of the intravenous course. There has been a most favorable outcome.

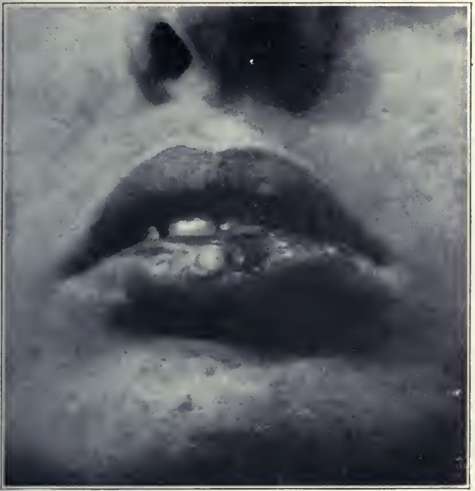

Fig. 1.—Recent chancre of lower lip. Spirochete pallida found in dark field.

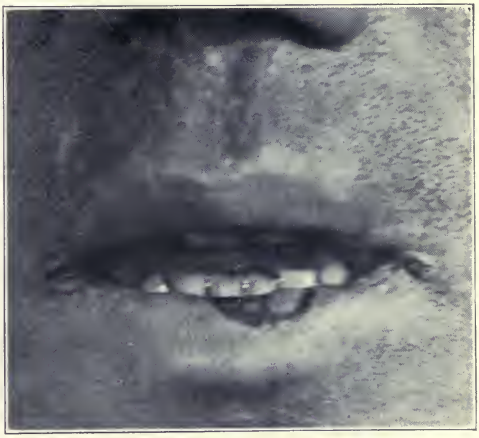

Fig. 2.—Healing chancre of lower lip with split papule of secondary syphilis at angles of mouth.

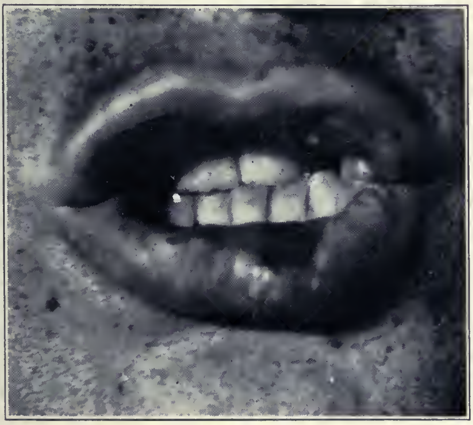

Fig. 3.—Chancre of lower lip.

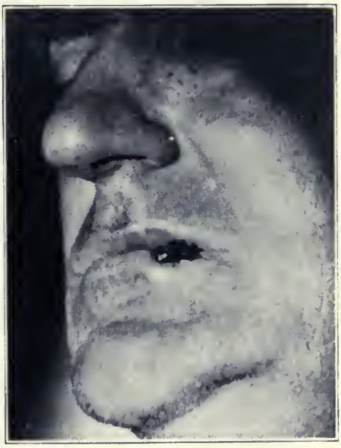

Fig. 4.—Chancre of lower lip. Compare with close up photograph in Fig. 5.

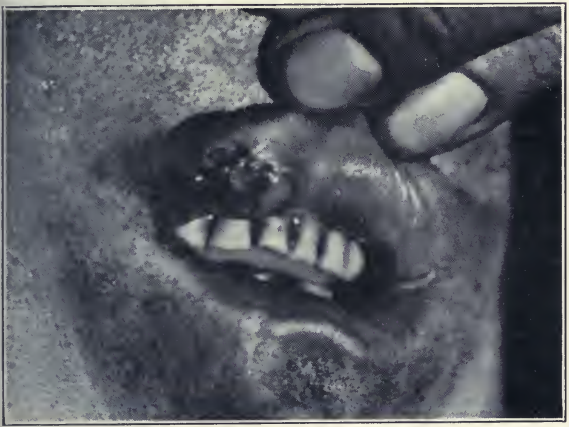

Fig. 5.—Chancre of lower lip. Same patient as in Fig. 4.

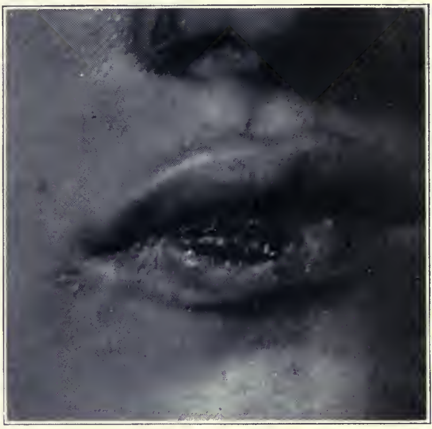

Fig. 6.—Chancre of lower lip.

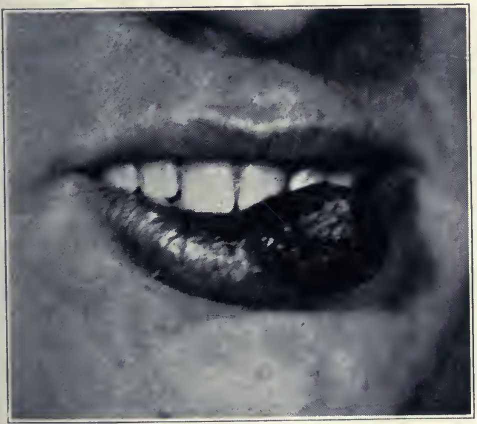

Fig. 7.—Chancre of lower lip. Case Mrs. H. K. (See text).

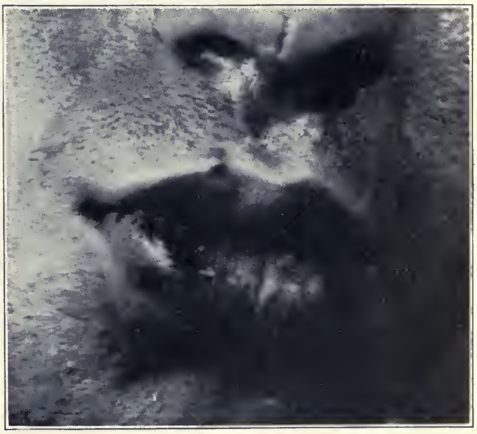

Fig. 8.—Multiple chancres of lips. Patient also had multiple genital chancres. Case W. K. (See text).

Another of our patients gave a very interesting story which is thought worthy of reciting. Mrs. H. K., aged twenty-eight, came to us with a history of sore of the lower lip of about two weeks' duration. She also complained of sore throat for about two days. She presented an indurated lesion on the lower lip, with cervical gland enlargement. The dark-field examination of the sore was positive for the Spirocheta pallida. The patient had been married eleven years. There was one child alive and well, and there had been one accidental miscarriage six months before. Her husband had always been well, but about sixteen days previously had noticed "cold sores". About a week before, his lip had bled following some trauma, since which time the lesions had ulcerated and bled easily. The submaxillary glands on the left side had been considerably enlarged, but were neither tender nor painful. There had been occasional headaches. The source of contagion for this family was not elicited.

Often it is indeed difficult to determine the mode of infection. For example, Mrs. H. K. was referred to us with a fading roseola, and condylomata and the active chancre still present on the lower lip, left side. She had been married five months and although her husband admitted syphilitic infection nine years before, no active lesions were discernible on our clinical examinations. Both had 4-plus Wassermann reactions. It is possible of course that the wife was infected by an osculatory relative or friend at her marriage ceremony and the husband being a latent syphilitic did not acquire a lesion from her. Such infections have been reported in the past.

Others of our patients, and they form the majority of the single women do not give any data regarding the possibility of exposure. One little recent immigrant girl, M. D., aged seventeen, lived with her parents and a host of male boarders. She presented herself at the clinic with a chancre of the upper lip, which had been present two months, marked secondary skin lesions of syphilis, and condylomata lata about the genitals. There was no evidence of genital chancre, nor any reason to suspect its possibility. The girl could not recall any one other than the immediate family who had kissed her. Since the family was not especially demonstrative, and not in the habit of kissing, they had agreed that the infection was probably acquired through the medium of some utensil used in common by the transient boarders and the family.

Mrs. I. S., aged nineteen, reported with the scar of a lip chancre which had been diagnosed by a positive dark-field examination for Spirocheta pallida at The Montreal General Hospital about 2½ months before. She had received a short course of arsphenamine and mercury, and her Wassermann was negative, and remained so while under observation and treatment for 18 months.

I. Ha., aged twenty-four years, knew that she had a lesion on the lower lip about seven weeks previously, to which little attention was paid by herself or physician. An eruption of secondary syphilis was the first warning that the lip lesion was other than a benign sore. The Wassermann was 4-plus and she received a course of injections of arsphenamine and mercury. One interesting phase of the cutaneous manifestations of syphilis in this patient was that she presented the leuco-melanoderma of leucoderma colli concomitantly with the roseola.

Mrs. I. Ho., aged nineteen, was another young woman who did not get any consideration regarding the possibility of a lip lesion being syphilitic until the secondary eruption suggested a Wassermann reaction and appropriate attention. At the time she came to us, she presented the remains of a chancre of the lower lip, a roseola and condylomata lata.

Among the men patients with chancre of the lip, the case of E. F., aged thirty-four, has been most interesting. The patient was sent to us with the story that he had had a canker sore on the lower lip, which had been treated locally some five weeks previously. About eight days after its appearance, the lesion began to swell, and pus was discharged. He had been given potassium iodide about three weeks before we saw him and the reason for his transfer for consultation was that a rash had appeared over the entire body, which was suspected of being an iodide eruption. The lesions of the wide spread cutaneous outbreak were varicelliform and on first impression the eruption was worthy of being considered the rash of iodide. The Wassermann reaction had been taken on two occasions previously and reported negative. The glandular enlargement of the cervical glands was not definitely that of an initial lesion. Another Wassermann was taken, the possibility of syphilis being present was reserved, and the patient told to call again. On the next visit, the clinical diagnosis of secondary syphilis was made, despite the fact that the Wassermann was only weakly-positive. The scar of the lip lesion was perfectly covered, and there had been no other mucous membrane lesions from which a successful spirochete search could have been made. Prior to the first intravenous injection, blood was taken for a 4th Wassermann and this was reported 4-plus. We have not satisfied ourselves regarding the cause of the slow development of the strongly positive Wassermann in this patient.

The source of infection in this man was not determined.

We have had few instances of chancre of the lip associated with similar lesion of the genitals. In J. F., aged twenty-four, we were given the following history: Six months before he had gonorrheal urethritis. About two months previously he had noticed a lesion on the under surface of the glans penis, and two weeks after that he had noticed that there was a denuded area on the lower lip right side, which did not heal. The lip lesion went on to ulceration. The lesion of the penis and that of the lip were present on his first examination. The glands of the draining areas were enlarged. An eruption of maculopapular syphilis had been present for one day and mucous patches of the left tonsil were noted. This patient had been to a dentist since the appearance of the lip lesion and the resultant adenopathy, and the dentist had removed a tooth, which he had thought to be the cause of the adenopathy. No change in the gland followed. It is idle to speculate as to the possibilities of mediate and intermediate infections from this patient through the nonrecognization by the dentist of the character of the lip lesion.

Another patient, W. H., aged thirty-two, with lesions of primary syphilis of the lower lip had multiple lesions of the penis. Dark-field examination of four lesions revealed the presence of Spirochete pallida in each. The Wassermann was 4-plus.

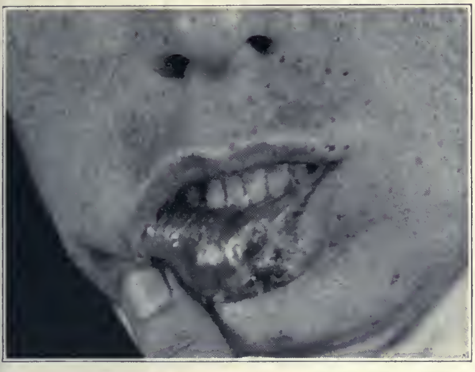

Fig. 9.—Ulcerated chancre of lower lip.

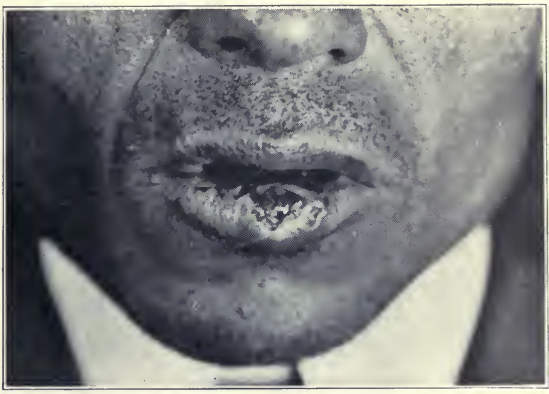

Fig. 10.—Ulcerated chancre of lower lip.

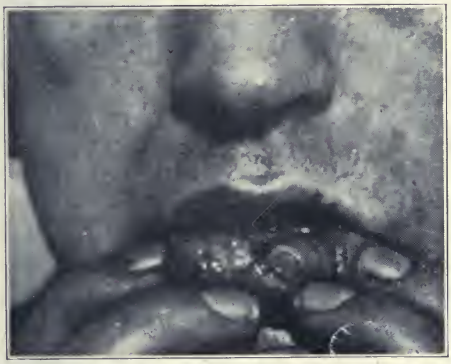

Fig. 11.—Ulcerated chancre of lower lip.

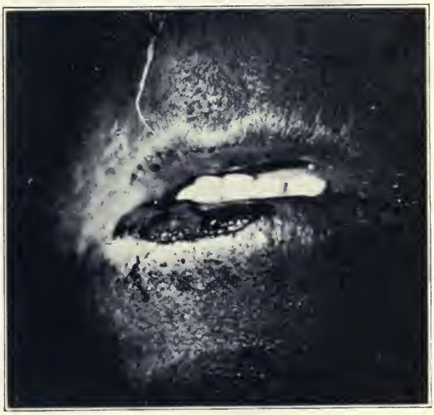

Fig. 12.—Crusted lesion of lower lip suggested epithelioma but was chancre.

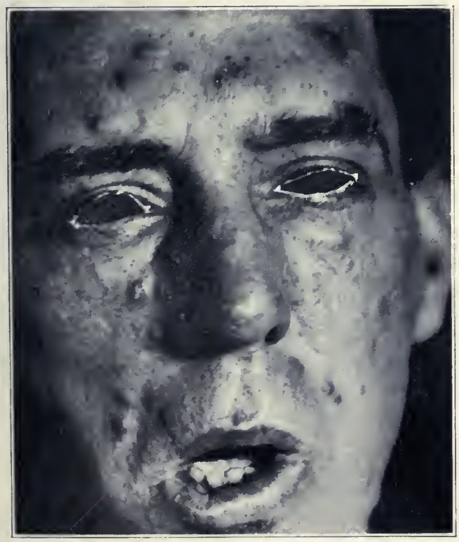

Fig. 13.—Scar of chancre of lip with secondary syphilis. Case E. F. (See text).

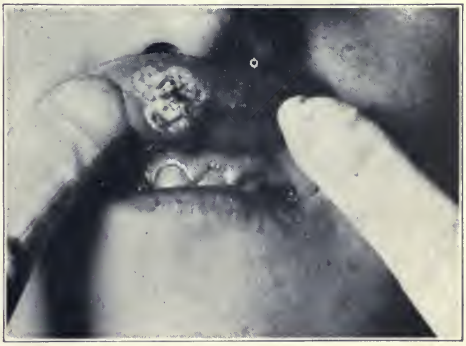

Fig. 14.—Ulcerated chancre of upper lip.

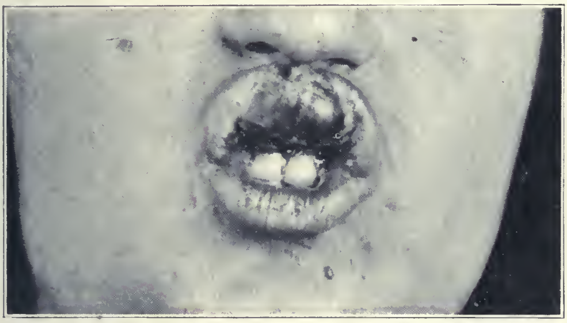

Fig. 15.—Late chancre of upper lip. Case M. D. (See text.)

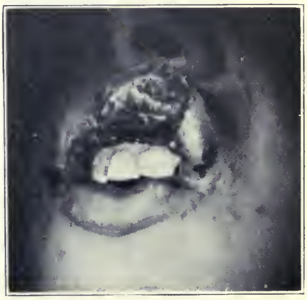

Fig. 16.—Late chancre of upper lip. Case of R. B. (See text.)

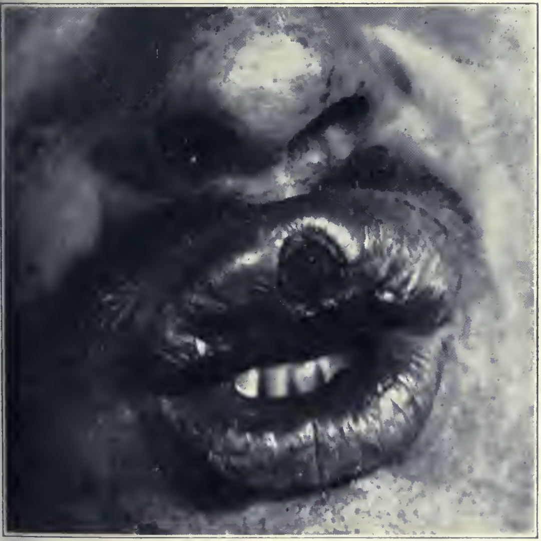

Fig. 17.—Ulcerated chancre of upper lip.

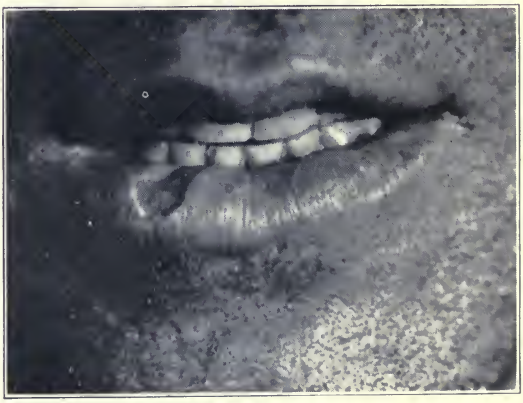

Fig. 18.—Scar of epithelioma treated by radium; lesion first mistaken for syphilis at another clinic and treated unsuccessfully with arsphenamin and mercury.

Mr. R. J. L., aged thirty-nine, single, came to the clinic with a chancre of the lower lip and a muscular papular syphilide, and moist lesions of the scrotum, and penis. He reported that he had noticed what he thought to be a canker sore on the lip for six weeks, and thought that he had bitten this sore which caused it to be infected. In this manner he sought to account for the difficulty in healing, and to abate his suspicions. He admitted exposure two weeks prior to the appearance of the canker sore.

Still another patient, E. D., aged twenty-five, came for treatment with the evidence of generalized syphilis manifested by a maculo-papular eruption, mucous patches and a positive Wassermann reaction. He denied having been exposed by intercourse for eleven months, but admitted having kissed a number of women. The lesion of the lip, which was still present showed the presence of Spirocheta pallida on dark-field examination. The glands in anatomical relation to this lip lesion were enlarged. The moral standing of this patient was not of the highest and he became a morphine habitue while still under observation. At one time he was using about five grains of morphine three times a day. The Wassermann reaction in this patient has been negative for over thirty months.

We present two other histories despite the fact that they are meagre. C. D., a widow, aged forty-five, came to the clinic with the evidences of an old right hemiplegia, and the degeneration associated with it. She claimed to have had a chancre of the lip some 20 years previously. The treatment early in the course of the syphilitic infection had been of the slightest even for those days. Since the hemiplegia, she had been given iodides and mercury and there had been some improvement. After a course of arsphenamine, the improvement in muscular motion was noted, but the patient did not persist in treatment.

A. R., aged thirty-seven years, came to the hospital with an ulceration of the lower lip, but no evidence of infiltration. The sore was said to have been present three months, and had been increasing in size. At another hospital, a Wassermann had been made, and reported 2-plus, on the basis of which, antisyphilitic treatment had been instituted. The patient had received 9 intravenous arsphenamine and 5 intramuscular injections. The fact that the lesion did not improve, but rather progressed with this course did not alter the procedure in the least, and further antisyphilitic treatment was to be given, when the patient reported to us. The diagnosis was rendered more simple for us, perhaps, than for the physicians who first saw him, as we could not conceive that a syphilitic lesion could resist the type and number of injections which the patient had received. The Wassermann, incidently, was still 2-plus. Treatment with radium cleared the lesion nicely. It was an epithelioma.

COMMENT

The number of histories could be increased, but in the main, those recited give the principal factors which make the primary syphilitic lesion of the lip an interesting and important one. As we see the problem of syphilis acquired by lip chancres, the patient, and the first physician consulted, if the patient goes to a doctor, has the ultimate fate of the case in hand. If syphilis is not suspected, and the stories related seem to prove that it is not, the patient goes on through the generalized period of syphilis, and all that pertains to it. The benign appearance of the early lip chancre is certainly deceptive, or else, the physician is loath to consider the possibility of such a diagnosis. In most instances, the picture of lip chancre as ordinarily illustrated in text books, seems a terrible lesion indeed, and one which could never be overlooked. Unfortunately, the lip chancre of syphilis does not always follow the text book, and as our own photographs show, many a harmless lesion harbors the Spirochete of syphilis, and unless checked by proper treatment, the course of syphilis runs on.

The dark-field and the Wassermann, but above all, clinical acumen and experience are needed for the diagnosis and ultimate abatement of the process of syphilis in the patient with a lip chancre.

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SYPHILIS AS WE SEE IT AMONG THE NATIVES OF BECHUANALAND TODAY

Being a Study of Some 1547 Cases of Syphilis Occurring among the Native Tribes of Taung, Extending over a Period of Six Years

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THIS contribution deals with a study of some 1500 cases of syphilis occurring among the native population of Bechuanaland in general, but more particularly among the natives of Taung—an extensive stretch of native territory in Bechuanaland, situated on the northwestern borderland of the Cape Province, Union of South Africa. The paper has as its object the setting forth of the nature of the disease among the native population of these districts, the points where it differs from European syphilis, its manner of transmission, and its powers of passage to the third or even fourth generations.

INTRODUCTION

The concensus of native opinion is that syphilis did not commence to make its appearance with rapidity and severity amongst the tribes in Bechuanaland until after the opening of the diamond fields, which drew continuously from the area for the ever-increasing labor requirements of the Kimberley Mines. The official reports in connection with Warren's Expedition in 1885, show that the natives were then badly affected, and the diseased condition of the prisoners taken towards the close of the Langeberg campaign, at Kuruman, is almost a matter of history. From that time onwards the prevalence of syphilis in these districts has been continually emphasized. If we disregard the possibility of some earlier infection, and take the commencement of labor activity in the diamond fields at about 1874 as the date of the wholesale introduction of the disease, there was until 1906, a period of over thirty years during which syphilis had had an almost unchecked spread among the native tribes of the area. Now the native population of Bechuanaland, excluding Gordonia, was, at the 1904 census, approximately 68,000. In 1909 in the districts of Mafeking, Kuruman, Taung and Vryburg, there were treated 2,367 cases of syphilis—or, in other words, 3.7 per cent of the entire population. We do not think that we should be far out if we state that at least 5 per cent of the entire native population of Bechuanaland are suffering from active manifestations of syphilis, and that the percentage of those actually tainted with the disease is considerably higher. In certain native ''locations'' in the Vryburg district it is believed that as many as 25 per cent of the inhabitants are afflicted.[1]

Since its introduction, which must be considered recent in comparison to its introduction elsewhere, syphilis is seen to be causing a perceptibly lowered vitality of the race, and evidence of race degeneration in Bechuanaland is abundant. Such races as the Batlapins and the Barolongs have suffered particularly. It would seem that the future product of these races will be a Bantu degenerate of a similar type to, but worse than, the mixed degenerate of the old coastal races, who may be found throughout South Africa today. The original Bechuana was not a man of stature, but he was a hardy well-built individual. Of this there can be no doubt at all. Today, it is the exception to see a fine adult specimen of either sex.

These races have not suffered as others have done from the encroachment of European influences and civilization. The majority still live under the direct control of their own chiefs, in their own large native areas, reserved to them by the Imperial Government in the Act of Annexation. As a race they have had everything in their favor under protective European government and guidance, and a marked racial improvement might reasonably have been expected. Yet it has been the reverse, and the explanation is clearly that of syphilization of the community. Syphilis plus degeneracy is all that the Bechuanaland native will be able to supply to the labor centres of South Africa.[1]

METHODS EMPLOYED IN CARRYING OUT THIS INVESTIGATION

Bechuanaland is mostly a vast stretch of arid veld on the border of the Kalihari Desert. Except for a number of small towns along the railway line, and the small township which has sprung up at the oasis of Kuruman, it is sparsely populated. Here and there we find a police outpost and widely-spread farm homesteads. Vast stretches are devoted purely to native reserve, and there no white man may farm. It follows, then, that hospital accommodation is scanty, facilities for carrying out investigation meagre and difficult, patients are compelled to travel long distances, and communication with the outside world is a rare and infrequent incident. Nevertheless the day is long and the amount of clinical material well-nigh inexhaustible.

Under provisions of Act No. 39 of 1885 (Cape of Good Hope), attendance for treatment of any person found to be suffering from venereal disease can be made compulsory on a magistrate's order. In the absence of hospital accommodation all patients were treated as outdoor patients, and the powers given in the Act just mentioned were made use of freely. On account of the very great distances which many of the patients had to travel, it was found, as a rule, impossible to see them more often than once a month.

A register of syphilitic patients was kept over a period of six years, of which the following is a summary:

No. of cases placed on the register	1827
No. of readmissions to the register	280
No. of original cases on the register	1547

Of this number, by following out the family history of each individual patient, family groups were framed. Where only one member of a family appeared he was, naturally, left ungrouped. We find, therefore:

No. of cases placed in 286 family groups	1009
No. of cases left ungrouped	538

It is often a matter of considerable difficulty to obtain a reliable family history from the native on account of the common custom of adopting children. Moreover the loose manner in which they use terms of relationship is confusing—for example, when a European indicates "cousin," the native speaks glibly of "brother" or "sister," or even "uncle" or "aunt." A further complication is the custom of the next eldest brother taking to wife his deceased brother's widow. As far as has been possible, however, by careful and repeated investigation all relationships have been expressed in European terms of affinity.

EXTRACT OF REGISTER

The following extract of the register compiled of syphilitic natives will give some indication of (1) the wholesale syphilization of families; (2) the preponderance of heredosyphilis; (3) the total absence of acquired syphilis; and (4) the type of lesion met with in these natives. It will also supply statistical details of individual cases referred to in the family trees presented and in the text.

It should be noted that the details given read continuously, as if the tabulation were written in one continuous line: e. g., ‘‘7 Varied ulceration body and limbs; daughter of

‘‘8 nasal gummata,’’ indicates that No. 7 is the daughter of No. 8, and so on.

REGISTER NUMBER	FAMILY GROUP	DETAILS OF SYMPTOMS AND RELATIONSHIP	OVER 14	UNDER 14	SEX
22	9	Gummatous ulceration knee and leg; sister of	x		F
23		Vaginal mucous plaques; sister of		x	F
24		Nasopharyngeal gummata; brother of	x		M
278		Pustular syphiloderm; cousin of	x		F
1700		Nasal Gumma; mother of	x		F
1701		Snuffles.		x	
1818		Anal scarring, nasal gumma; cousin of 22.	x		F
40	15	Psoriasiform syphiloderm; mother of	x		F
268		Buccal mucous plaques; *“wit-kop”*.	x		F
54	20	Pharyngeal ulceration; aunt of	x		F
55		Gummatous ulceration foot; daughter of	x		F
202		Nasal Gumma; husband of	x		M
203		Nasopharyngeal ulceration; mother of	x		F
204		Mucous plaques; sister of		x	F
205		Nasal ulceration.		x	F
57	21	Pustular syphiloderm; father of	x		M
68		Nasal necrosis; cousin of	x		F
219		Nasopharyngeal ulceration; cousin of	x		F
1187		*“Wit-kop”;* brother of		x	M
1436		Pustular syphiloderm scalp; sister of		x	F
1791		*“Wit-kop”;* cousin of		x	M
1189		*“Wit-kop”;* cousin of		x	M
1188		*“Wit-kop”;* brother of		x	M
1534		*“Wit-kop”;* cousin of		x	M
1533		*“Wit-kop”;* cousin of		x	F
218		Pustular syphiloderm; cousin of		x	M
1767		Nasal necrosis.	x		F
58	22	Broken-down gumma knee; niece of	x		F
1719		Pustular syphiloderm; niece of	x		F
76		Psoriasiform syphiloderm; cousin of	x		M
1356		Nasal gumma.		x	M
61	24	Gummatous ulceration of legs; mother of	x		F
1734		Periostitis and synovitis knee; brother of	x		M
742		Gummatous ulceration of shoulder; mother of	x		F
1429		Pharyngeal ulceration and syphiloderm; cousin of		x	F
62		Nasopharyngeal ulceration; sister of	x		F
99		Buccal mucous plaques; cousin of		x	M
690		Iritis; sister of		x	F
1401		*“Wit-kop”,* pharyngeal ulceration;		x	F
1407		Rhinitis, adenopathy; nephew of 61			M
72	29	Gummatous ulceration of left ankle; cousin of	x		M
73		Gumma of elbow; niece of	x		F
880		Nasopharyngeal ulceration; aunt of	x		F
1723		Nasal necrosis; cousin of	x		M
1724		Mucous plaques, anal ulceration; brother of		x	M
1725		Mucous plaques, syphiloderm; brother of		x	M
1809		Facial and buccal necrosis; nephew of 880	x		M
881		Nasopharyngeal ulceration; cousin of		x	M
1535		*“Wit-kop”*.		x	F

REGISTER NUMBER	FAMILY GROUP	DETAILS OF SYMPTOMS AND RELATIONSHIP	OVER 14	UNDER 14	SEX
82	31	Gumma of knee; mother of	x		F
220		Pustular syphiloderm; sister of	x		F
530		Nasal ulceration, later *"wit-kop"*; niece of	x		F
980		Nasopharyngeal ulceration; aunt of	x		F
1045		*"Wit-kop"*; cousin of	x		M
1686		Nasopharyngeal ulceration; cousin of	x		F
1123		Tibial periostitis, later *"wit-kop"*; cousin of		x	M
1298		Pharyngeal ulceration; cousin of	x		F
1530		*"Wit-kop"*.		x	F
85	32	*"Wit-kop"*; brother of	x		M
86		Nasal ulceration; brother of	x		M
87		Nasal ulceration; brother of	x		M
88		*"Wit-kop"*; son of		x	M
89		Nasal necrosis; husband of	x		M
90		Nasal necrosis; mother of	x		F
91		Mucous plaques; brother of	x		M
362		*"Wit-kop"* and multiple scarring; cousin of		x	F
294		Nasopharyngeal ulceration; brother of		x	M
1815		Tibial periostitis; cousin of		x	F
1184		Nasopharyngeal ulceration; cousin of		x	F
1561		Carpal periostitis; brother of		x	M
1567		*"Wit-kop"*; brother of		x	M
1568		*"Wit-kop"*.		x	M
124	40	Syphiloderm, later *"wit-kop"*; sister of	x		F
125		Syphiloderm, later *"wit-kop"*; sister of	x		F
126		Syphiloderm, later *"wit-kop"*; sister of	x		F
127		Syphiloderm, later *"wit-kop"*; brother of	x		M
128		Syphiloderm, later *"wit-kop"*; brother of		x	M
129		Ulcerating double inguinal bubo; later *"wit-kop"*; mucous plaques; brother of		x	M
130		Syphiloderm, later *"wit-kop"*; brother of	x		M
131		Syphiloderm, later *"wit-kop"*.		x	F
145	44	Pustular syphiloderm and gummata; sister of	x		F
423		Nasal ulceration, later *"wit-kop"*; sister of		x	F
424		Nasal ulceration, later *"wit-kop"*; nephew of		x	M
1425		Buccal and labial necrosis; father of	x		M
1246		*"Wit-kop"*.		x	F
148	45	Nasal pharyngeal and facial ulceration; aunt of	x		F
398		Leucoplakia; sister of		x	F
428		Nasal ulceration; sister of	x		F
429		Nasal necrosis; brother of		x	M
430		Nasal ulceration and mucous plaques; sister of		x	F
431		Mucous plaques; brother of		x	M
432		Nasal ulceration; brother of		x	M
1787		*"Wit-kop"*.		x	M
1048		Pharyngeal ulceration; cousin of 148	x		F
1376		Nasal ulceration; cousin of 148	x		F
161	50	Syphiloderm and mucous plaques; brother of		x	M
162		Syphiloderm; sister of		x	F
163		Syphiloderm; sister of		x	F
384		Pharyngeal ulceration; cousin of	x		M
383		*"Wit-kop"*; cousin of		x	M
1109		Hydrocephalic dwarf, ulceration chest; cousin of	x		F
371		Gumma of elbow, synovitis of knee; mother of	x		F
1594		Nasal ulceration and *"wit-kop"*; cousin of		x	F
187		Syphiloderm; sister of		x	F
1812		Nasopharyngeal ulceration, anal scarring; child of		x	F
186		Pharyngeal ulceration.	x		F
709	89	Pains in body and limbs, pharyngeal congestion; father of	x		M
298		Mucous plaques, later *"wit-kop"*; brother of		x	M
1167		Mucous plaques, later syphiloderm; brother of		x	M
1351		Mucous plaques chiefly buccal.		x	F

REGISTER NUMBER	FAMILY GROUP	DETAILS OF SYMPTOMS AND RELATIONSHIP	OVER 14	UNDER 14	SEX
1369	93	Pustular syphilides of face; husband of	x		M
314		Nasopharyngeal ulceration; mother of		x	F
1414		*"Wit-kop"*; sister of		x	F
412		Leucoplakia, gumma of buttock; sister of		x	F
555		Mild nasopharyngeal ulceration.		x	M
397	110	Gumma of ankle; daughter of	x		F
400		Ulcerative labial necrosis; mother of	x		F
401		Nasal gumma; uncle of	x		M
402		Nasal ulceration; child of 397; brother of		x	M
403		Multiple gummata; brother of		x	M
404		Nasal ulceration, later *"wit-kop"*; brother of		x	M
405		Nasal ulceration, later *"wit-kop"*.		x	M
446	117	Nasopharyngeal ulceration; mother of	x		F
562		Nasopharyngeal ulceration; mother of	x		F
447		Buccal mucous plaques; sister of	x		F
448		Mucous plaques, anal condylomata.		x	F
510	130	Facial and nasopharyngeal necrosis; son of	x		M
949		Papulo-tubercular syphiloderm; grandfather of	x		M
570		*"Wit-kop"*; sister of	x		F
572		*"Wit-kop"*; cousin of		x	F
571		*"Wit-kop"*.		x	F
544	135	Nasopharyngeal ulceration, syphiloderm; brother of		x	M
679		*"Wit-kop"*; half-sister of		x	F
567		*"Wit-kop"*; brother of		x	M
1174		Tibial periostitis; second cousins to		x	M
568		Nasal ulceration, later *"wit-kop"*; brother of		x	M
739		*"Wit-kop"*; second cousins to		x	M
569		*"Wit-kop"*; brother of		x	M
882		*"Wit-kop"*; cousin of		x	M
564		*"Wit-kop"*; brother of		x	M
565		*"Wit-kop"*; sister of		x	F
566		*"Wit-kop"*.		x	F
1663		Nasopharyngeal gumma; uncle of above	x		M
846		*"Wit-kop"*; mother of	x		F
1643		*"Wit-kop"*.		x	M
691	154	Gumma of knee; mother of	x		F
784		Breaking down gumma of ankle; sister of		x	F
785		Nasal ulceration; brother of		x	M
1084		Nasopharyngeal ulceration; sister of		x	F
1683		Nasal ulceration; niece of	x		F
1017		Nasopharyngeal ulceration; sister of 691; wife of	x		F
1153		Iritis; father of	x		M
1163		Iritis, and nasopharyngeal ulceration; brother of		x	M
1224		Nasopharyngeal ulceration; sister of		x	F
1684		Nasopharyngeal ulceration; sister of		x	F
1693		*"Wit-kop"*.		x	F
934	191	Ulceration of breasts; mother of	x		F
935		Nasal ulceration, later *"wit-kop"*; sister of		x	F
936		Nasal ulceration; brother of		x	M
1647		*"Wit-kop"*.		x	M
938	193	Fibroid Phthisis and old scarring; cousin of	x		M
939		*"Wit-kop"*; brother of		x	M
1515		*"Wit-kop"*; brother of		x	M
1516		*"Wit-kop"*; sister of		x	F
1517		*"Wit-kop"*; sister of		x	F
1518		*"Wit-kop"*; sister of		x	F
1519		*"Wit-kop"*; cousin of		x	M
1641		*"Wit-kop"*; cousin of		x	M
1642		*"Wit-kop"*; cousin of		x	F
1775		*"Wit-kop"*; sister of		x	F
1776		*"Wit-kop"*.		x	M
1186	217	*"Wit-kop"*; sister of		x	F
1240		*"Wit-kop"*; daughter of		x	F
1573		Breaking down gumma of thigh.	x		M

REGISTER NUMBER	FAMILY GROUP	DETAILS OF SYMPTOMS AND RELATIONSHIP	OVER 14	UNDER 14	SEX
1336	230	Breaking down gumma of thigh; mother of	x		F
1337		*"Wit-kop".*		x	F
1357	234	Nasal and aural gummata; grandson of		x	M
1359		Nasopharyngeal gummata; husband of	x		M
1360		Nasopharyngeal ulceration; grandmother of	x		F
1373		*"Wit-kop";* brother of		x	M
1374		Nasal necrosis; cousin of	x		M
1375		Nasopharyngeal ulceration; cousin of	x		M
1415		Vulvar and axillary condylomata; daughter of	x		F
1416		Nasal ulceration and fibroid phthisis.	x		F
1597	255	Chancre and secondary exanthem; husband of	x		M
1612		Vulvar condylomata; mother of	x		F
1613		Nasal ulceration and *"wit-kop";* sister of		x	F
1722		Nasal ulceration.		x	M
1694	267	*"Wit-kop";* uncle of		x	M
1695		*"Wit-kop";* cousin of		x	F
1817		*"Wit-kop".*		x	F
318	283	Breaking down gumma of buttock; cousin of	x		M
319		Breaking down gumma of buttock; father of	x		M
328		*"Wit-kop";* brother of		x	M
552		Nasal ulceration; cousin of	x		F
340		*"Wit-kop";* nephew of		x	M
321		Nasopharyngeal gummata; mother of	x		F
322		Nasal ulceration; brother of	x		M
332		Tibial periostitis; cousin of		x	M
1670		Nasal necrosis; sister of	x		F
1757		Pustular syphiloderm; cousin of		x	F
336		Synovitis knee; cousin of 319; brother of	x		M
342		*"Wit-kop"* and syphiloderm; cousin of	x		F
337		*"Wit-kop";* sister of		x	F
338		*"Wit-kop";* brother of		x	M
339		*"Wit-kop";* cousin of		x	F
1799		*"Wit-kop";* sister of		x	F
1800		*"Wit-kop"* and palatine necrosis; cousin of		x	F
1758		*"Wit-kop".*		x	M
335	284	Fungating granuloma of nose; brother of	x		M
546		Nasal necrosis; brother of	x		M
329		Gumma of neck; mother of	x		F
330		Nasal ulceration and *"wit-kop".*		x	F
320		Breaking down gumma of leg; cousin of 329	x		F
341		Pharyngeal ulceration; cousin of 320	x		F

SYPHILIZATION OF FAMILIES

During this investigation the extensive syphilization of whole families has become apparent. From the figures just given, it will be noted that the proportion of grouped to ungrouped cases is roughly two to one. That is to say, of all the cases of syphilis handled during the period under survey, 67 per cent belonged to families of which other members were syphilitic. Surely this fact alone, indicates the great prevalence of the disease and its extraordinary ramifications in families.

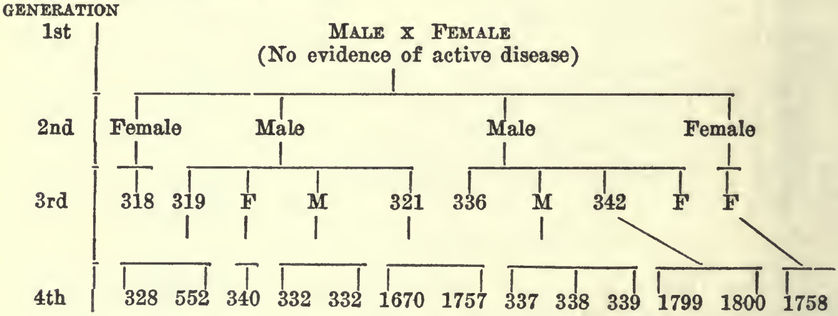
Of the cases apparently not linked up in family connection, and therefore ungrouped, one must not conclude that they have no family history of syphilis. Sooner or later such evidence is forthcoming as fresh cases come up for survey. A good example of this will be found in Group No. 9, where Cases Nos. 22, 23, 24 and 278, admitted in the year 1906, were found to be related to Case No. 1700 which was admitted in 1911, although for this period of five years no luetic family history had been obtained.

The extraordinary family syphilization which has taken place among this native population is well illustrated in the register (pp. 3-7). For purposes of following out histories of individual cases it may be well to mention that cases were put on the register as follows:

1st year	Nos. 1 to 945
2nd year	Nos. 946 to 1184
3rd year	Nos. 1185 to 1425
4th year	Nos. 1426 to 1581
5th year	Nos. 1582 to 1677
6th year	Nos. 1678 to 1827

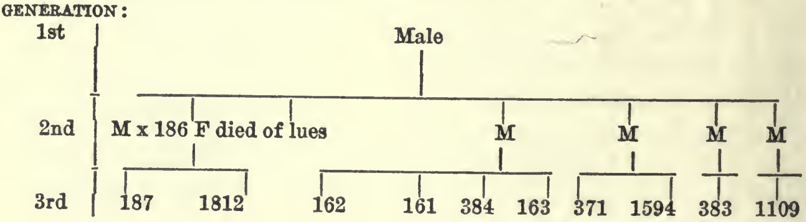
FAMILY TREE No. 1

This family tree which concerns family group No. 283, and is closely related to family group No. 284 (also syphilitic) illustrates the widespread nature of familial syphilis in Bechuanaland. The numerals employed correspond to the case numbers in the register, and details of these cases may be found by consulting the register (pp. 3-7). Only those members of the family indicated by numerals are proved syphilitics.



FAMILY TREE No. 2

This family tree concerns family group No. 50 in the register, and shows the extraordinary widespread syphilization of whole families. All these cases are heredo-syphilitics, and the numerals again correspond with their case numbers in the register.



POSSIBLE MODES OF TRANSMISSION

To have a clear conception of the colossal family syphilization which has been going on among these natives during the last fifty years, particularly in light of the evidence of this investigation, it may be well to discuss briefly the possible methods of syphilis transmission, considering therewith such secondary etiologic factors as climate, race, idiosyncrasy, immunity, sensitization, occupation, modes of living, and racial customs. The following methods must be considered:

(1) Sexual promiscuity.
(2) Syphilis d'Emblée.
(3) Syphilis insontium.
(4) Intermediate contagion.
(5) Unnatural sex practices.
(6) Hereditary transmission.

(1) *Sexual promiscuity.*—The whole question of sexual contagion is one which requires the most careful consideration, and is modified to a great extent by the question of whether we are dealing with the disease in its hereditary aspect, or as affecting the first generation. To uphold the view that syphilis in Bechuanaland is mainly acquired, and that due to sexual contagion, one must be prepared to admit that gross immorality exists, and has existed, among the Bechuanas, for by no other means could sexual contagion have produced the wholesale infection which exists today. The length of time that the disease has existed among these people therefore would have to be ignored.

While sexual promiscuity is the chief method of spread of the disease among white peoples, it is impossible to come to the same conclusion when dealing with the Bechuanaland native. It is the fact that a primary chancre—and particularly a genital sore—is something of a pathologic curiosity in these districts, as indeed it is in many other native areas in South Africa (McArthur and Thornton,[1] Mehliss, Garrow,[2] de Vos Hugo,[3] Reith Fraser,[4] and many others). We therefore are sadly lacking in evidence of any sexual spread of the disease.

(2) *Syphilis d'Emblée.*—This term is applied to acquired syphilis where no known primary chancre has been found. Probably in the vast majority of these cases the primary lesion has been so

small and insignificant that it has been overlooked, and when healed has left no scar. On the other hand cases of true syphilis d'Emblée have been put on record, where no primary lesion has preceded true secondary syphiloderms (Jullien,[5] Hutchinson,[6] McDonagh.[7] While we are unable to bring forward evidence that this phenomenon is more common among the Bechuanaland natives than among white peoples, its possibility is sufficiently alluring to warrant further investigation, at any rate among the small proportion of the disease which might truthfully be described as acquired.

(3) *Syphilis insontium.*—By this we mean innocent nonsexual infection. Many examples are on record, including the victims of a circular kissing game (Shamberg[9]) and numerous cases of the infection of European children in South Africa by native nurse girls. Possibly extragenital infection occurs more frequently than is generally supposed. Delinotte[10] records that in the hospitals of Bordeaux 192 extragenital chancres occurred as compared with 703 genital lesions over the same period, or 1 extragenital to every 3.6 genital chancres. In certain parts of Southeastern Europe the ratio of extragenital to genital chancres may be as high as 20 to 1 (McDonagh).[11] This is due to the conditions under which the people live, and here we have something of a parallel to the native of Bechuanaland. In addition the native has many curious customs about which we know little, which may give to syphilis insontium a greater significance than it has in the incidence of European syphilis. The possible combination of syphilis d'Emblée and syphilis insontium may afford further explanation of the rarity with which extragenital chancres are seen (particularly in other parts of South Africa where acquired syphilis is more common than in Bechuanaland). Even if the chancre were evident, however, it is doubtful if the native would bring it to notice or seek advice concerning it. We are of opinion, however, that heredosyphilis is so prevalent that even these methods of transmission just mentioned have little scope among the Bechuanaland natives.

(4) *Intermediate contagion.*—Examples of intermediate transmission of syphilis are furnished by the pedestrian who was infected by the flick from the lash of a passing syphilitic teamster (Melot[8]), the seven glass-blowers (Brosius) and many more usual cases of infection transmitted by eating utensils. Experience in Bechuana-

land shows that case-to-case infection without sexual intercourse gives rise to the major portion of such acquired syphilis as is met with. The amount of direct evidence in support of this is very considerable, and cannot be disregarded. The reason for this spread is due doubtless to the dirty habits and customs of the people. Among them it is usual for the pipe to travel from one to the other; their eating and drinking utensils are shared in common; clothing and bedding are treated in the same manner, and in many domestic habits they are constantly risking contagion.[1] Were heredosyphilis, with its undoubted partial immunity, less common, it is conceivable that the intermediate transmission of acquired syphilis in these native areas would be appalling.

(5) *Unnatural sex practices.*—Contrary to much popular belief, sexual promiscuity is not the rule among the native. In his own way he is not without a standard of morality, and the virginity of his maidens is held in very high esteem. Nevertheless he indulges in many revolting and ribald sex distortions which pass unchallenged. Many of these depend on manual and corporeal manipulation and the bastardizing of sexual function. *"Metcha,"* a practice where the axilla or thighs of a young child are employed by the adult male to secure sexual gratification, is a good example of the waywardness of the native's moral creed. It is possible that the disease may frequently be transmitted in this manner. Reith Fraser has reported three cases where primary chancres in this part of the country were apparently caused in this manner.[4]

(6) *Hereditary transmission.*—It is unnecessary to discuss hereditary syphilis here, for its ravages in white communities are too well known. Acquired syphilis in infancy, however, is exceedingly difficult to differentiate from the hereditary variety, and its possible occurrence must not be overlooked. Even in European syphilis its incidence is more frequent than is generally supposed. Cases of infants infected by wet-nurses, and by feeding bottles, spoons, and the like are well known, while contagion from adults also occurs. Contagion from lesions of the maternal genitalia during the process of parturition must be exceedingly rare, chiefly on account of the protection afforded the foetus by the *vernix caseosa.* Lomholt,[12] however, cites two cases from literature and puts on record three cases from his own practice.

The contagiousness of hereditary syphilis must be considered a factor in the spread of the disease, particularly when one remembers the domestic conditions of the natives' home life. It has been said that the contagiousness of hereditary syphilis has been overstated, but the fact remains that the Spironema pallidum is readily demonstrable in the lesions of heredosyphilis, and the positive clinical evidence of Fournier and the experimental evidence of Neisser are conclusive. That hereditary syphilis is essentially contagious, therefore, is an established fact. On account of the extensive familial syphilization, however, this danger is practically limited to strangers, in Bechuanaland.

THIRD GENERATION TRANSMISSION

The possibility of transmission of syphilis to the third generation has been the subject of long controversy. Conclusive evidence is scanty, for human beings cannot be caged, interbred, and watched like animals. The advocates of third generation transmission include Finger[32] and Fournier,[33] but Hutchinson regarded the evidence of his earlier cases inconclusive, and later in his career disbelieved in such transmission. Gaucher,[34] on the other hand, records a case of transmission to the fourth generation. While few investigators have the good fortune to be able to follow up cases through three generations, the Bechuanaland native who was living more or less on one's doorstep has afforded the writer many such opportunities—potential if not absolute. Generally speaking it is difficult to exclude an intervening genitor, and any interruption of the chain destroys much of the value of the evidence. Proof of parentage, also, strictly speaking, is impossible to obtain. All evidence submitted, therefore, must be presumptive rather than positive.

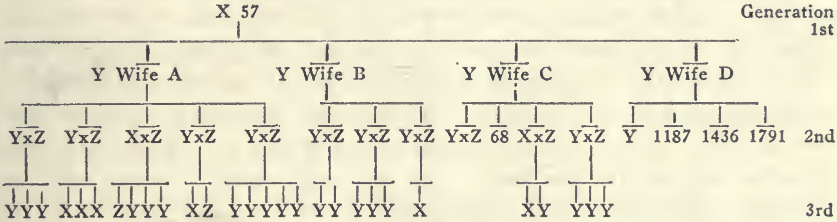
While one appreciates the possibility of reinfection in a heredosyphilitic (the *binary syphilis* of Tarnowsky[30] supported by the authentic case of Jullien,[31] such a reinfection has never been established in the series of cases under review. Nevertheless one presents the following family trees with the utmost diffidence, knowing full well that it is the easiest thing in the world to refute the absolute value of these observations were it not for the fact that comparison with acquired syphilis, second generation syphilis, and either of these complicated by other congenital anomalies, is well-nigh convincing even in the absence of any trace of absolute proof (Fig. 1). Moreover acquired syphilis in Bechuanaland is a comparatively unusual occurrence so far as one's observations are concerned. It would seem an unfair argument were we to assume that the vast bulk of acquired infection occurred among those already affected with heredosyphilis, and that, also, without any evidence of its occurrence. Moreover such acquired syphilis as is met with conforms to the classical descriptions of the disease as met with in Europe and elsewhere, and in no way resembles the atypical disease so common among the natives under review.

FAMILY TREE NO. 3

This family tree is presented on account of the presumptive evidence it furnishes regarding the transmission of syphilis to the third generation. To suggest that in every case where an intervening parent is unknown a syphilitic genitor was introduced in the second generation would mean nothing less than wholesale whoredom, together with an exceedingly high incidence of acquired syphilis among the Bechuanaland natives. That neither of these circumstances obtain we are well aware. The presumption is, then, that unknown genitors were either healthy individuals or heredosyphilitics.

This tree concerns the family history of Case No. 57, group No. 21, showing the syphilitic affections of his wives, children, and grandchildren. This case, a chief of his tribe, contracted syphilis from his wife B in the year 1890.

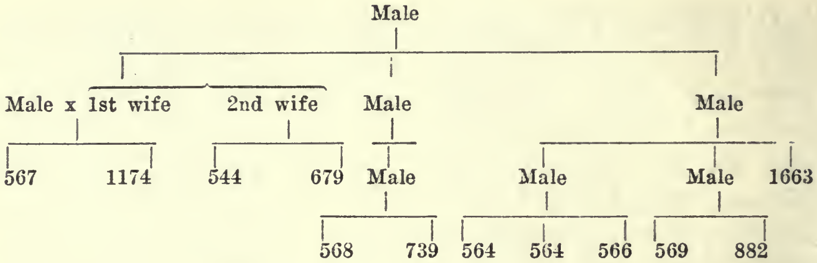
The numerals correspond to the case numbers in the register. The following signs are employed: X indicates syphilitic infection, Y indicates no apparent disease, and Z indicates syphilitic state unknown.


X 57
Generation 1st
Y Wife A
Y Wife B
Y Wife C
Y Wife D
YxZ YxZ XxZ YxZ YxZ YxZ YxZ YxZ YxZ 68 XxZ YxZ Y 1187 1436 1791
2nd
YYY XXX ZYYY XZ YYYYY YY YYY X XY YYY
3rd

It will be seen that in the second generation there are six known heredosyphilitics, and in the third generation six cases of heredosyphilis.

FAMILY TREE NO. 4

The following family tree which concerns family group No. 135 is interesting on account of the fact that every member of the third generation or his descendants is a heredosyphilitic. Group No. 130, comprising a father, son, and the latter's three nieces, all suffering from heredosyphilis, belong to the same common stock. The numerals again correspond to the case numbers in the register.



SYPHILIS OR FRAMBESIA TROPICA

In some quarters the doubt whether the disease we see in the South African native is syphilis or frambesia tropica has been entertained seriously. Arguments in favor of the frambesia view were put forward by de Vos Hugo,[3, 13] and a fierce controversy raged in the subsequent South African Medical Press.[14] Since frambesia tropica has been established as a distinct disease,[15] it may be well to settle this point for all time.

Yaws is a specific disease of the tropics, characterized by a frambesiform eruption, highly contagious, and generally believed to be due to the *Treponema pertenue* (Castellani[16]). Its geographical distribution is said to include Rhodesia and South Africa, occasionally among Kaffirs (Macleod[17]). Among Europeans it is exceedingly rare, and is confined almost entirely to natives, where its spread is fostered by insanitary dwellings and overcrowding. While it is most common among children, it may occasionally occur at any age. One attack does not produce any absolute immunity, and reinfections are frequent. This is one important point of differentiation between this disease and syphilis. Others of still greater import are that it is not transmitted by heredity, and is seldom seen under six months of age.

The primary stage is characterized by an incubation period of two to four weeks, general toxemia accompanied by fever, joint pains and headache, an initial lesion of coalescing papules invariably extragenital, and eventually a dry crust which leaves an ulcer and frequently a granulomatous nodule. The secondary stage appears some six weeks later, and is very much more severe in its general manifestations than the similar stage in syphilis. Crops of tiny papules which eventually form moist warty masses which dry up and crust, form the typical picture. These crusts when removed leave raw papillomatous lesions which are the typical yaws. In old standing cases the skin exhales a characteristic fusty aroma. Painful ulceration of the soles (*crab* yaws) with its peculiar gait, nail changes, hyperkeratosis, neuritis, and tropic changes complete the picture. The mucous membranes are as a rule peculiarly immune, and adenopathy and eye changes are infrequent. The tertiary stage may appear many years afterwards. Granulomatous ulcers, suppurating gummatous nodules, and hypertrophic scarring, are most characteristic.

At this point one cannot do better than quote the summing up of the position as regards Bechuanaland by McArthur and Thornton[1]: "It is, we think, probable that the difficulty in finding initial lesions has been the reason why the question of the disease being really yaws has been raised. It is hard to understand how any similarity between the two diseases can be claimed. In no way do the symptoms coincide with those of yaws, as recognized elsewhere. There is no regularity of symptoms; there is not the regular age incidence, the itching, the peculiar smell, or the heaped up crusts of eruption, and there are very few cases indeed which do not react promptly to mercury in some form. On the contrary, there is the primary sore in certain cases, the adenitis, the exanthem, the alopoecia, the bone and eye affections, the polymorphism of the eruptions, and the gummata, and, finally and conclusively, there are the hereditary features of the disease as we see them today in these native districts." The following two cases, selected at random, show a characteristic picture of syphilitic disease, and could not be seriously taken as suggestive of *Treponema pertenue* infection.

Case 1.—This case is characteristic of much of the syphilitic disease in Bechuanaland, and indicates the response to salvarsan and mercurial medication. Male native, aged 30 years, of good physique, came under treatment in March 1912. He presented numerous large gummata of the neck with much swelling and superficial ulceration and breaking down of tissue. In May, 1912, after less than two months oral mercurial treatment, he showed gummatous swelling in the neck, with four healed scars on the left side. These are said to have been active in 1905, when he was treated for a time in Kimberley General Hospital. A large gummatous mass was also present over the right sterno-mastoid muscle, a healing broken-down gumma at the inner extremity of the right clavicle, and a similar sore over the thyroid region. In addition three broken-down gummata were apparent on the left side of the neck. There were no other signs of spironemal activity. In May of that year 0.5 gramme salvarsan was administered, and the following is his condition four months later: the improvement which followed the injection of salvarsan has been maintained, the large gummata have disappeared, and the ulcerations have either healed or become very much reduced in size. A few indurated nodules remain about the sides of the neck. His general condition improved, and oral administration of mercury and potassium iodide was continued.

CASE 2.—This case is thought worthy of report to show the value of salvarsan in the treatment of these destructive lesions in the native. On account of the great distances to be covered, the lack of railways and transportation, and the ignorant and uneducated condition of these peoples, it is only possible to treat them with mercurial preparations. The carrying out of the treatment rests entirely with the native himself, and it is therefore usually spasmodic. Were it possible to administer a few doses of salvarsan as a routine in these cases, and thereafter continue uninterrupted mercurial medication, much ghastly tissue destruction would be averted.

Masadimarope Macobane, female native, aged 35 years, came under observation in February, 1908. In spite of more or less continuous oral mercurial and potassium iodide medication, the following was the clinical picture in May, 1912: there is extensive gummatous ulceration of the cheeks, chin, and nose, affecting the whole mask of the face. Indeed, the whole surface is covered with dry encrustations, ulcerations, and pustules. Otherwise the woman is apparently healthy. After a single dose of 0.3 gramme salvarsan the response was immediate, the facial gummata began to heal, and the pustules ameliorated. Some four months afterwards, however, the improvement ceased and the active process again asserted itself. Had facilities for administering further salvarsan been available it is certain that the whole condition would have cleared up and remained healed.

IS REINFECTION EVIDENCE OF CURE OR FREEDOM FROM HEREDITARY TAINT?

We must be prepared to admit that reinfection is not conclusive evidence of curability. Jacobi has reminded us that, in the present state of our knowledge, it is impossible to state whether the cure of syphilis is relative or absolute.[18] The binary syphilis of Tarnowsky is also admitted to occur[31] which would indicate that the immunity conferred by hereditary transmission is not absolute. Moreover, Morrow[19] has written that reinfection in acquired syphilis is an acknowledged fact, and that in some cases the surface manifestations of a former attack were plainly evident and coincident with the eruptive phenomena of the second infection. Much must depend, however, on the make-up of the patient and the severity of the first attack.

How far immunity, relative or absolute in the heredosyphilitic is influenced by *Diday's law of decrease* is difficult to determine. It is possible that the survivor of an early pregnancy may be absolutely immune, while a later child of the same mother (having benefited, possibly, by the formation of maternal antibodies, or, according to Routh,[20] by the action of the chorionic ferments) may inherit only a partial and inadequate immunity. Treatment of the parents may also play a part in determining the heredoimmunity curve, although the type of parental disease seems to have but little effect.

It is well to bear these points in mind when drawing conclusions from the facts presented by this investigation. Nevertheless, over so large a series of cases, with such unusual family ramifications, one has failed to find any evidence of reinfection, or of any heredosyphilitic acquiring a subsequent infection.

VARIATIONS IN SYMPTOMATOLOGY BETWEEN EUROPEAN SYPHILIS AND THAT IN THE BECHUANALAND NATIVE

In investigating such a mass of cases and histories a good deal of valuable evidence is obtained regarding variations in the behavior of the disease in the native as compared with the European. These variations have undoubtedly an important bearing on heredosyphilis in the native. After a number of years' experience amongst various types of South African natives, one has long held the views that variations in the manifestations and effects of the disease existed. Doubtless other observers have noticed these variations but unfortunately one finds but little reference to the subject in literature. Zimmerman,[21] however, gives an interesting study of syphilis in the Negro of Baltimore. He notes the relative infrequency of extragenital infection, the severity of osteoarthritic manifestations, the frequency of eye symptoms, and the high incidence of follicular and pustular syphiloderms. The annular papular syphiloderm is so common as to reach the dignity of a racial peculiarity. Tertiary bone syphilis is predominant, and the rarity with which neurosyphilis occurs is emphasized. Marshall[22] gives a useful extract from Jeanselme touching on "exotic syphilis" which has many points in common with what one meets with in native syphilis in South Africa.

There is no doubt that on account of racial peculiarities one meets with a mass of contradictions and variations as compared with text-book standards of symptomatology in syphilis, and the question naturally arises as to why the disease should show these altered characteristics in native races. Explanation is difficult, and speculation is perfectly futile. It would seem, however, as a general principle, that the disease attacks the weakest organs—that is to say, those which are submitted to the greatest strain and most active metabolism. It follows that the cerebrospinal axis will be most unlikely to be attacked, and one finds this is so. The digestive apparatus, also, is never severely taxed in dealing with the native's simple and unchanging diet, and one would be surprised to find severe visceral syphilis. Again this is one's experience.

Speaking generally, both as regards acquired and hereditary disease, the severity of the constitutional attack in the native is rarely so severe as in the European. Malignancy is most uncommon. Constitutional disturbance in debilitated natives and in the bastard colored races is seen at times, but it is not the rule and is slight in comparison with the severity of the lesion. While the actual localized lesion may be exceedingly severe, the general upset is invariably infinitesimal. Thus it is no uncommon incident to find a native with, for example, extensive necrosis and gummatous ulceration carrying on his ordinary avocation. Except when inconvenienced or under compulsion, he is quite unconcerned about treatment, and so it will be found with many other severe conditions. (Fig. 2.)

Thus we find the type of lesion in the native varying from that in the European. In addition we also find the utmost variance of the type of lesion and the course of the disease among the natives themselves. This fact becomes very apparent when dealing with large numbers of cases, and is in itself interesting both in its bearing on the heredotransmission of the disease, and as a departure from orthodox ideas and teaching.

In acquired syphilis one doubtless gets fairly typical stages and symptoms, but it is not at all unusual to find, quite independent of treatment, an irregular sequence of symptoms from the earliest stages. Cases may jump from the initial chancre to a so-called tertiary manifestation. There is moreover, a constant overlapping and occurrence of what in the ordinary way would be called secondary and tertiary exhibitions.

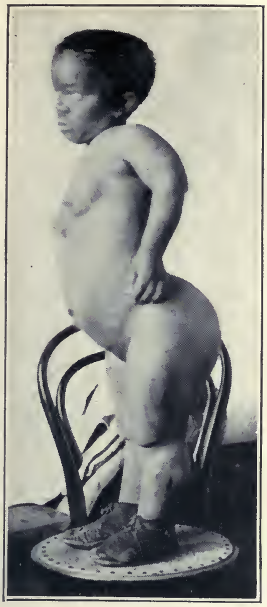


Fig. 1.—A hydrocephalic dwarf (Case No. 1109, Family Group No. 50). An excellent example of dystrophic anomaly. Her height, which could be measured in inches, may be judged by the relative size of the chair.

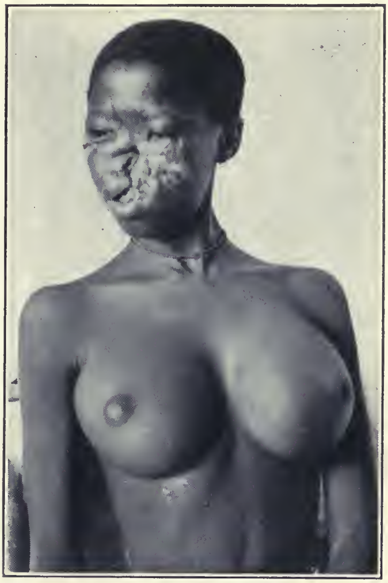


Fig. 2.—This case illustrates well the wonderful maintenance of general nutrition in spite of very longstanding, untreated, destructive syphilitic lesions. (This girl is not pregnant, neither is she lactating.)

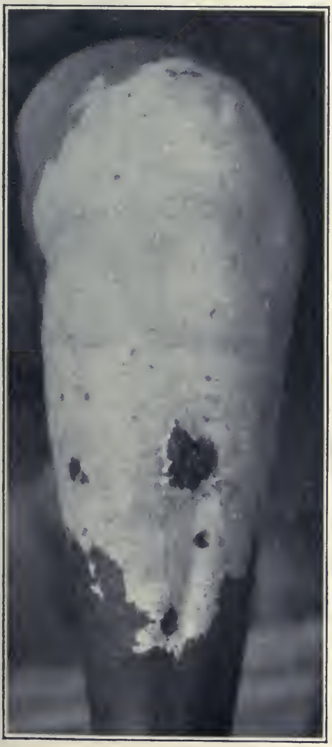


Fig. 3.—A youthful lesion which has long since gone on to latency. Such vitiliginous patches are typical of old syphilitic scarring in the native.

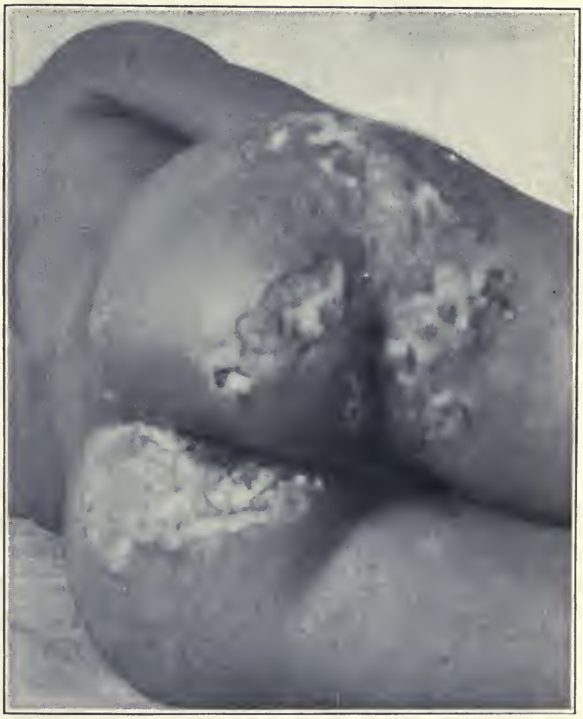


Fig. 4.—A good example of the chronic isolated lesion. The buttock is a favorite site for pustulation superimposed on devitalized gummatous tissue.

One also meets a type of case where it is difficult, and indeed often impossible, to say whether the disease is acquired or hereditary. In cases presumably acquired, one finds constantly exhibited stationary conditions of the lesions such as one finds in heredosyphilis. On the contrary, the latter class, at all ages, may exhibit lesions indistinguishable from those which might have been acquired in origin. The family groups show that the majority of the cases are hereditary, but of the minority one cannot say definitely that they are acquired, chiefly on account of the difficulty in obtaining reliable family histories. Many of these cases are either known to be individual instances of hereditary syphilis, while others show only the similarity in type with no supporting history.

This variation in symptomatology to which we have referred, leads to difficulty in differentiating between the two types. From one's observations some of the more interesting points in these features of native syphilis are these:

(1) Absence of visceral lesions.

(2) Absence of neurosyphilis.

(3) High incidence of *syphilis hereditaria tarda:* (*L'hérédo-syphilis tardive*).

(4) Chronicity of isolated lesions.

(5) A favoid condition of the scalp and its relation to syphilis: (*wit-kop*).

(1) *Absence of visceral lesions.*—This is quite an evident feature in these people as in other native races. Amongst all one's cases one has noted only two instances where obscure internal symptoms pointed to gummata. With an experience of a large number of postmortem examinations among natives, one has not yet found a gumma of the viscera.

The remarkable integrity of the viscera in native syphilis perhaps accounts for the continued virility of these natives under aggravated conditions of disease which would prove incapacitating or even fatal to the European. Not only do they carry on their usual avocations, but propagation is unhindered and seldom interrupted by abortion or miscarriage. Active lesions in the female do not seem to foster miscarriage. So it follows that these natives are assured of offspring, which, after all, is the end-all and be-all of their existence.

Since Brock[23] drew attention to a lung condition which he found frequent among syphilitic South African natives, one has particularly investigated this point. He described a particular apical affection which he found in 35 per cent of his cases, but one has not found such a lesion in anything like the proportion that he reports. One agrees, however, that there is a marked tendency to lung affection. This one has observed for a very long time, the usual lesion being of the character of an interstitial fibrosis of irregular distribution and situation. Cases frequently develop a cough without fever but with slight expectoration which is rarely blood-stained. On physical examination one finds areas of dulness, diminished breath sounds, and dry rather than moist râles. Taken early, vigorous treatment quickly clears up this condition, and leaves little to be detected except patches of slight dulness and altered breath sounds. Other cases again, exhibit all the symptoms of a pleuritic attack. Various postmortem examinations on natives often have revealed, with and without known luetic histories, signs of old pleurisies and fibroid changes in the lungs, sometimes accompanied by small healed cavities. One has, however, had no opportunity of observing changes at autopsy in a case where the lung condition had been active at the time of death. From the above it is evident that in native syphilis there is to be found at times a not very active form of specific pulmonary fibrosis.

Colleagues in neighboring districts have had similar experience, a fact which is of considerable importance in connection with the spread of native tuberculosis. The native suffering from syphilis whether it be hereditary or acquired is prone to develop tuberculous pulmonary lesions, either with a slow, insidious onset, most frequently seen in syphilitics of long standing, or with an acute and rapidly fatal course which occurs in the more severe types of nasopharyngeal and laryngeal syphilitic lesions.

One has found much evidence of this latter condition at autopsy, in cases where death had occurred from hemoptysis. No doubt the pulmonary fibrosis, as Brock has suggested,[23] is a factor of the first importance in determining this fatal termination. Pulmonary tuberculous disease is making rapid strides among the natives races in South Africa, and the significance of syphilis as a predisposing etiologic factor cannot be overlooked. There is ample evidence of this among the degenerates of the bastard half-breed races of

South Africa. The history of their syphilization dates back to the early days of coastal settlement, and their susceptibility to pulmonary tuberculous disease is a fact well recognized. It would indeed be a short-sighted policy to ignore the possibilities of broadcast tuberculous infection taking place among those native races, already degenerate, now in process of syphilization.

(2) *Absence of neurosyphilides.*—Implication of the cerebrospinal axis in the native is practically unknown. One has met with only six cases with pronounced nervous lesions, and tabes dorsalis and dementia paralytica have never been seen. This rarity of neurosyphilis among native races has been previously noted, and various speculative reasons have been advanced in explanation. Those usually mentioned are the absence of alcoholism and freedom from nerve strain. Discussing syphilis in Egypt, Madden[24] says "That it seems as if the disease burnt itself out in its primary and secondary stages," and tertiary symptoms are uncommon. This may be an unfair parallel, for syphilis in Northern Africa dates back many hundreds of years, and it is probable that these people have survived their ancestral syphilization with a larger share of immunization than sensitization. It is the fact, however, that the so-called tertiary stage in the Bechuanaland native is uncommonly severe and destructive, even if his deep viscera and cerebrospinal axis apparently escape. The incredible amount of heredosyphilis would also suggest that there is no exhaustion of the virus, and little in the way of immunization either relative or absolute. This is possibly due to the fact that the process of syphilization started so recently in the history of the races concerned.

Freedom from alcoholism as a probable explanation of the apparent immunity of the cerebrospinal axis does not carry us very far. In these parts alcohol is the bane of the native's life. He indulges overfreely in the beer he brews—a beverage by no means impotent—and this he fortifies on every possible occasion with foreign spirit. In the towns, or whenever opportunity occurs, his main object is to get systematically drunk.

Again it is not enough to suggest that the disease among these peoples is benign, or that they show unusual tolerance to the disease. They have failed to show tolerance to many other diseases such as smallpox, while they have successfully acquired the European's partial immunity to measles and scarlet fever.

It is generally acknowledged that the Spironema pallidum is prone to attack weakened tissues. The European certainly uses his central nervous mechanism more than does the native, and the bustle and worries of our modern civilization possibly add to the general strain to which the European's cerebrospinal axis is submitted. It would appear, then, that this circumstance might help to explain the immunity of the native to cerebrospinal syphilis. That it is only part of the explanation, however, is clear on further inquiry. Other factors materially affect the issue, chief of which is the question of antibody formation. For many years native syphilis was absolutely untreated, and even at the present time there are vast numbers of infected natives, chiefly in the so-called *Native Reserves,* who receive no treatment at all, or at best only scanty and inadequate medication. Moreover, where treatment has been carried out systematically, it has consisted solely of oral mercury and potassium iodide. These drugs, as we know, do not inhibit antibody formation, and these patients have been flooded with a plentiful supply of antibodies over long periods of years which apparently has proved sufficient to guarantee the adequate protection of the cerebrospinal axis. The cerebrospinal axis which, as we know, derives its main antibody supply from the general systematic circulation, has been bathed in antibodies since the early days of the primary infection and any stray or enterprising parasite has been afforded little opportunity to do harm. This fact, if taken into consideration, together with the previous statement that the cerebrospinal axis is intact and has at no time been submitted to strain of any kind, may be sufficient to explain the immunity of the central nervous system in spite of (or rather, perhaps, in virtue of) the extreme destructive severity of the so-called tertiary cutaneous lesions.

That treatment methods afford a large part of the explanation is further borne out by the experience of Mehliss[25] to whom is accredited the statement that neurosyphilides of even the mildest variety have only appeared among South African natives since the introduction of arsenobenzene into the treatment routine. If therefore the arsenobenzine-treated native is liable to exhibit a neurosyphilide, we have strong additional evidence that the type of treatment has much to do with the determining of the negligible incidence of cerebrospinal syphilides. In view of the work of Wile and Stokes[26] who declare that the fate of every syphilitic as regards his cerebrospinal future is determined in the first months of the infection, an investigation into spinal fluid changes in early native syphilis would be exceedingly instructive. Reith Fraser[27] sums up the position admirably in the following sentence: "In the natives of South Africa the mild primary stage which is characteristic, and which is frequently absent, is due to a lack of local cell reaction around the attacking organism and not to any inherited immunity. The cell reaction is seen in the generalization stage when cutaneous syphilides are particularly severe. The antibody mobilized at this period seems to act as a bulwark of defense for the nervous system, which subsequently is never involved to an extent sufficient to produce clinical symptoms."

(3) *High incidence of syphilis hereditaria tarda.*—The vast amount of hereditary syphilis is one of the most striking features of native syphilis in Bechuanaland. Speaking generally one is most impressed with the puny condition in infancy of syphilitic children as compared with the youth of nonsyphilitic tribes. This leads in after life to a degree of arrested development not amounting to infantilism but effecting a marked diminution of physique. There is no constancy in appearance of the many text-book signs of heredosyphilis. One may look in vain for "*the triad of Hutchinson.*" Keratitis is seen occasionally, but specific deafness is unknown. Hutchinson's teeth simply do not exist, but Wall's mulberry molar[35] is met with in practically every case (Reith Fraser). The "saddle nose" is often in evidence, but then that is also a type of physiognomy. Amongst the more frequent manifestations are mucous plaques, condylomata, tibial periostitis, and "*wit-kop*" —a favoid condition of the scalp, which will be discussed in detail later.

The incidence of *syphilis hereditaria tarda* is exceedingly high. In glancing through the family groups on pages 3-7, it is apparent, by following the enumeration of the individual cases how seldom members of the same family have been placed on the register at the same time. One's procedure was always, if possible, to examine all immediate members of a family from which a case had come. It was not often that one found more than one or two cases at that time, and yet later on—it might be a matter of several years—some of the other members of the family would come under treatment with symptoms quite recently developed. One finds, therefore, that irregular outbreaks of hereditary syphilitic manifestations occur in families at any period from infancy even up to full adult and marriageable age. In fact one is beginning to suspect that many cases appearing at later periods verging on middle life are instances of *syphilis hereditaria tarda.*

The evidence of any former lesions is quite uncertain in these cases of late heredosyphilis. In some it will be found, while in others it is definitely absent. When such evidence is present it is rare to find that there has been any previous treatment. There is no doubt that in such cases with signs of lesions in infancy or early youth, the condition went on spontaneously to latency. (Fig. 3.) In others a clinical cure would seem to have taken place. Of this one has numerous examples. Symptoms and signs appearing later on in life are clearly hereditary, and there is no question of reinfection. There are many examples of such cases in the family groups, but it is unnecessary to cite more than one.

The reader is referred to family group No. 89. All the members of the family were examined in 1906. No. 298 in the group was found to show mucous plaques, but no affection of any other member of the family could be found. Six months later the father was treated for a rheumatic or influenzal attack, having symptoms of pyrexia, malaise, and general pains. He did not improve under the usual antirheumatic treatment measures, and, showing some pharyngitis, he was placed under mercurial medication, with the result that the symptoms cleared up. He was kept under the influence of the drug for a long period, and has since shown no further signs. About the time that he was put on mercurial treatment No. 298 showed early signs of *"wit-kop."* In June, 1908, a brother aged 12 years, was brought with mucous plaques and a varioloid rash which was generalized. In June, 1909, a sister aged 6 years, was brought for treatment and found to be suffering from mucous plaques, and has since developed *"wit-kop."* The man's wife has shown no evidence of active syphilis at any time. Moreover, the children must surely be examples of *syphilis hereditaria tarda.* Were it otherwise, some evidence of primary infection would have been discovered. Yet it must be borne in mind that they were all the offspring of syphilitic stock. In family groups Nos. 15, 117, and 135, among many others, there are particular instances of the first ap-

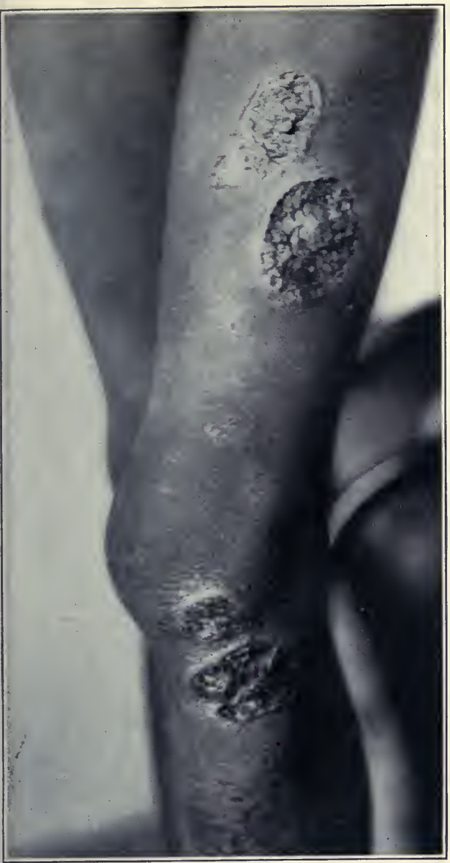


Fig. 5.—This photograph illustrated a typical non-progressive isolated lesion—untreated. The situation, size, and character are typical.

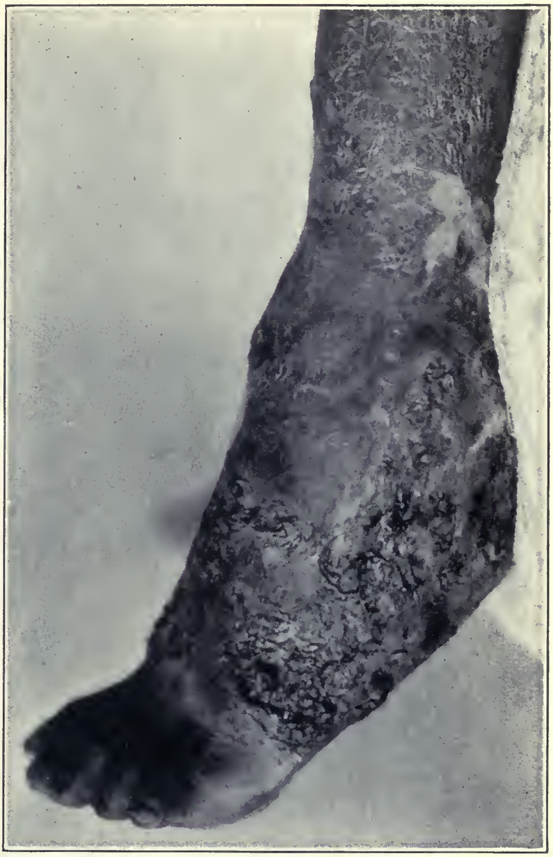


Fig. 6.—A characteristic chronic isolated lesion which, if met with elsewhere, would undoubtedly be diagnosed a tertiary manifestation.

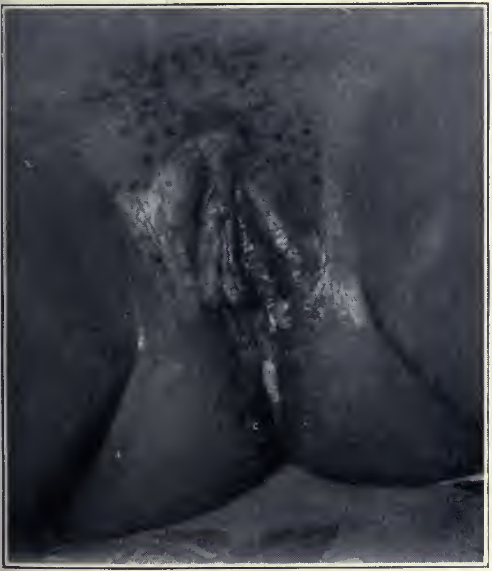


Fig. 7.—Photograph of the genitalia of Case No. 1612, who infected her husband after she had borne him two syphilitic children.

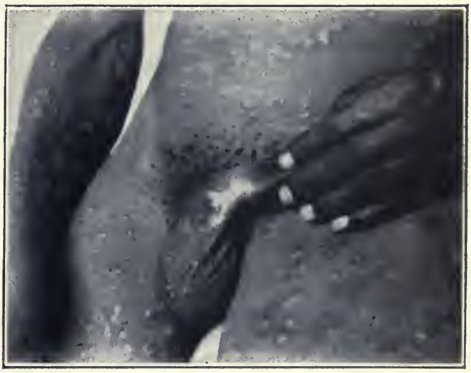


Fig. 8.—This photograph shows the healing chancre scar and the typical secondary eruption of Case 1597—the husband of Case 1612, illustrated in Fig. 7.

pearance of the disease in adult life, with younger members of the family already affected.

In many of the family groups there is no direct parental history. This may be considered strange and unlikely, but the fact that maternal syphilis is so frequently latent and symptomless must not be forgotten. In spite of this, however, the vast majority of such cases must be considered examples of *syphilis hereditaria tarda* for these reasons: (1) lack of evidence of acquired infection, and (2) the discovery of other members of the family showing active lesions at some later date. Whether there is a parental history or not, the similarity of symptoms in such cases is very striking. It is therefore impossible to ignore the question of hereditary infection in explaining these irregular outbreaks of syphilis in families. It must be noted that at times one may be deceived as regards family history through the facts being hidden. An example in point will be found in family group No. 217. Two girls of adult age were found to be suffering from "*wit-kop,*" and no family history was obtained. Two years later, however, the father (case No. 1573) was brought up for treatment with much difficulty and found to be suffering from a lesion of many years' standing.

In spite of the exceedingly high incidence of heredosyphilis, abortions and miscarriages are rare, and infant mortality is in no way abnormal. The acquired and the hereditary syphilitics marry and are given in marriage. It is more or less an every day occurrence for an hereditary syphilitic to marry a syphilitic also hereditary; for an acquired syphilitic to marry an acquired syphilitic; for an hereditary syphilitic to marry an individual who has acquired his disease; and for a healthy normal individual to marry a syphilitic, either acquired or hereditary. In spite of this alarming state of affairs, these people propagate with regularity, commendable frequency, and precision. Their children are syphilitic; they grow to maturity, and proceed to do likewise. Thus we are faced with the problem not of solving the result of introducing a syphilitic genitor into a healthy family tree, but of introducing an acquired or hereditary syphilitic into a family tree already well syphilized. We find examples of hereditary syphilitics intermarrying throughout three or four generations, where it is quite the exception to have an untainted or an acquired syphilitic genitor introduced. In spite of this syphilization going on through generations, the fetus successfully maneuvres his intrauterine life and comes out in the open a full-blown syphilitic who can boast of his spironemal history going back three or four generations on both his paternal and maternal sides, without the blemish of an untainted healthy ancestor! Moreover he develops as a true heredosyphilitic should, and shows a generous proportion of the signs and symptoms of his kind. In turn he marries a heredosyphilitic mate, and their children present the same luetic characteristics. In other words, the passage of generations may serve to modify the disease, but it does not stamp it out.

In the face of so much evidence one must certainly ponder over the possibilities of third generation transmission. As has been pointed out there are plentiful examples of long-standing lesions in heredosyphilitics, and also numerous instances of latent heredosyphilis. Lesions will thus be found to be active and virulent at the procreative age, and the possibilities of offspring from such parents are undoubted. Indeed living offspring from such parents have been met with frequently in one's own experience.

According to Tarnowsky many of these cases would probably be regarded as examples of "binary syphilis." One has been unable, however, to obtain any conclusive evidence of reinfection. We have to admit a certain amount of laxity in native domestic life, but with the widespread disease which is encountered, one would also have to suggest nothing short of wholesale immorality to account for the reinfection of these numerous heredosyphilitic genitors. One is aware that it is not easy to disprove reinfection, but some evidence must have been forthcoming, and yet one cannot note even a suspicion of this having occurred amongst all the cases which have passed through one's hands. Another point which has to be borne in mind is that native syphilitics do not bear out some of the most important conclusions of Tarnowsky regarding the possibilities of third generation transmission. There is no evidence of heredosyphilis being responsible for much abortion, miscarriage, or stillbirth. The dystrophic effects of hereditary syphilis are very variable, and are often absent. Moreover there is no marked intensity of symptoms in the second generation. The objection that hereditary syphilitics with active disease are unlikely to marry does not apply to the native. Such an actively infective parent may propagate children showing active or latent syphilis, and it is certain that infant mortality among such progeny is by no means excessive. One has to remember also that the disease has existed for many years in these districts, and formerly was practically untreated. Yet there is no evidence to show that there is any appreciable diminution of the population from its effects, or, what is most crucial, the evidence of sterility and dying out of families.

Constitutionally, as has been shown, the native does not suffer as the European. He maintains his virility in spite of the most destructive lesion, and with good food and a little nursing he will often be able to rid himself of an active lesion without the aid of any specific treatment whatever. This was proved by a parallel series conducted at the Kimberley General Hospital by Russell. It is difficult to see how the possibilities of third or subsequent generation transmission are to be denied. Even the possibility makes one regard the future of the Bechuanaland native with apprehension.

(4) *Chronicity of isolated lesions.*—It is a common occurrence for adults of all ages to be placed under treatment with such conditions as advanced nasopharyngeal ulceration of many years' standing, showing little more than a very slowly-progressing tissue destruction. Amongst other single manifestations frequently met with are grouping of various forms of pustular syphilides about the elbows, knees, thighs, and buttocks. (Fig. 4.) The latter is a particularly favorite situation, and the pustules are generally implanted in a mass of gummatous tissue. There are also to a lesser extent other lesions exhibiting a similar isolation and chronicity. These isolated lesions are found to have existed for years; (Fig. 5.) they are so slightly progressive as to be almost stationary; they give rise to little inconvenience; bodily health is unimpaired; there has been no treatment of any kind in the majority of cases; and there have been no concurrent lesions. There are also more youthful cases, undoubtedly hereditary, which will be found to exhibit a similar chronicity and isolation of lesions.

Investigations as regards the adult cases point to this peculiarity of manifestations as being more of a feature of heredosyphilis, for there is to be obtained the evidences of lesions which have occurred at quite youthful ages. In particular, there are two which are very distinctive, namely, signs of an old "*wit-kop,*" and the deep scarring left by former mucous plaques. It may be objected that this scarring of the mucous membranes is possibly the site of a healed primary lesion, but the situations are too varied and the instances too numerous for this objection to be entertained. Even if it were true, there would still remain the peculiarity of a succeeding isolated lesion. With or without such signs, there is often a history of ''sores'' in youth. In contradistinction to the latter, one comes across a certain number of cases with old chronic lesions which give a clear history of an earlier acquired origin, previous treatment, other lesions and healed conditions. There are, however, the numerous instances with no history to guide one, and the question to be solved is whether one is dealing with hereditary or acquired disease. In the younger and known hereditary cases one meets the same conditions of long-standing lesions. The comparison makes one strongly of opinion that most of these doubtful adult cases are in all probability examples of *syphilis hereditaria tarda*.

One is aware that a condition such as described, when met with in adult natives living in towns, is classed usually as secondary or tertiary manifestation of acquired syphilis. (Fig. 6.) In a rural district, however, there is every opportunity of studying family history—a privilege denied to the town worker. Moreover there is also to be found the exact similitude of secondary and tertiary lesions in the native heredosyphilitic of all ages. Personally one does not meet with many cases having a clear history or evidence of acquired disease, early or late, and it is a remarkable fact already pointed out, how very few primary lesions are ever seen amongst these people.

The migration of natives from country to town and *vice versa* is continual, and in view of the vast amount of acquired syphilis in towns there should be ample evidence of primary infection among the natives under review. The writer does not deny that such is to be found there, but one considers that all doubtful cases must be regarded as hereditary in nature, more especially if they should come from a recognized syphilized district, or a known syphilitic family.

A study of the progeny of syphilized families is instructive. It is soon apparent that the children of the acquired syphilitic are most actively affected, and show a high death-rate in infancy and youth. Such families, however, are very much in the minority. The children of families syphilized in previous generations show

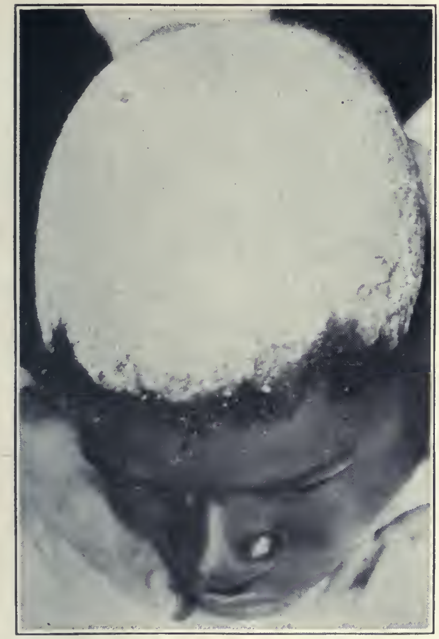


Fig. 9.—A fully developed case of *wit kop.* The typical white skull cap with its surrounding fringe of hair is well shown.

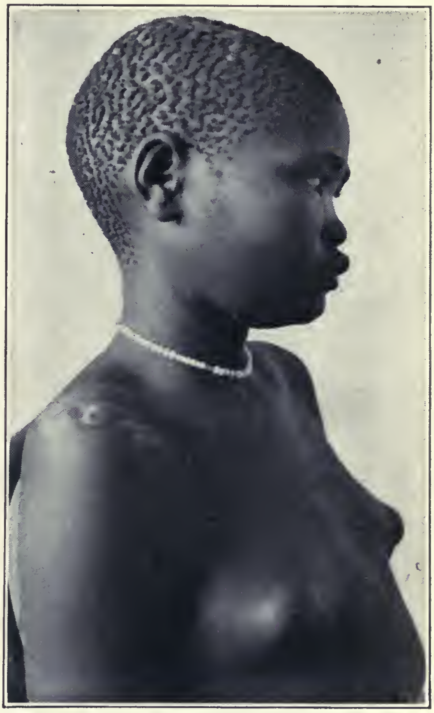


Fig. 10.—Photograph to illustrate *wit kop* in its earliest stages. The commencing lesion will be noticed high up on the scalp near the vertex. Other syphilitic stigmata are evident on the shoulder.

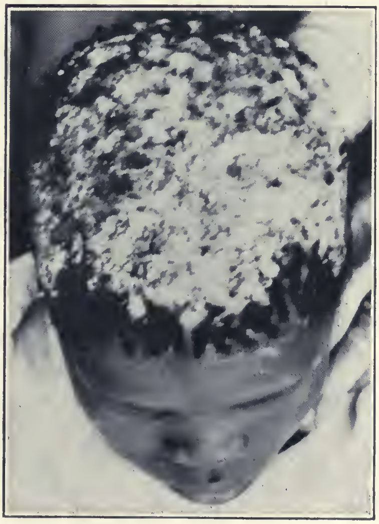


Fig. 11.—*Wit kop* scalp undergoing antiluetic treatment. The new growth of hair between the crusts is apparent.

much irregularity in the type and date of onset of symptoms. Many members of such families show definite clinical signs of syphilitic infection sooner or later, while others remain clinically free. Among the heredosyphilitics showing clinical manifestations in early life, the chronicity of individual lesions is especially marked, and it is rare to see any of this class showing rapid developments of the disease. Tissue destruction may be extensive and disfiguring, but it is never rapid. This is in marked contrast to the untreated acquired syphilitic in the so-called tertiary stage of the disease.

Considering all these points one cannot but incline to the belief that this peculiarity of manifestation is associated with hereditary disease, and not with that which is acquired. One may cull as additional evidence the fact that acquired syphilis as seen in the town native presents a typical primary genital focus, characteristic secondary exanthem with certain racial peculiarities, and a text-book tertiary stage with extensive and rapidly-destructive cutaneous and bony lesions showing their typical tendency to relapse. Since the general employment of arsenobenzene medication, also, we have much evidence that the native is now exhibiting active implication of his cerebrospinal axis.

The infectivity of such long-standing lesions is undoubted, and one has many examples of tertiary and old hereditary lesions proving contagious. Case No. 417 is an instance in point where a youth was infected by contact with a heredosyphilitic. Another instance is a girl friend of case No. 22 in family group No. 9 who slept with, and shared the blankets of this case. She appeared in due course exhibiting a typical Hunterian chancre on the inner surface of the thigh. Yet another example is case No. 1597 in family group No. 255 who became infected from his wife, case No. 1612 She was a heredosyphilitic who had had active lesions in her youth, and had borne him two syphilitic children before he eventually became infected. (Figs. 7 and 8.)

In the ordinary way, one would expect such lesions as mucous plaques and condylomata to be fruitful sources of infection. One can produce only a few examples, however. This is explained by the fact that there is so much familial hereditary syphilis that fresh virgin soil to receive the infection is difficult to find. When Europeans or half-breeds come in contact with these natives, however, they are, as one would anticipate, readily infected. Case No. 129 in family group No. 40, was responsible for infecting a half-breed boy by lending him his mouth organ. The former was suffering from buccal mucous plaques at the time, and the latter promptly developed a labial chancre. One recalls the case of a native heredosyphilitic exhibiting vulvar condylomata, who successfully infected a European. There are, moreover, many tragic examples of European children becoming infected by native nurse girls.

(5) *"Wit-Kop."*—One approaches with some diffidence the question of propounding anything new in the symptomatology of a disease such as syphilis. Nevertheless there are some interesting features in the condition about to be described which make it worthy of special remark. (Fig. 9.) The attention of the medical profession in South Africa was first directed to this condition by McArthur and Thornton in 1910.[1] It is a syphilitic condition of the scalp, most frequently seen in hereditary syphilis, but occasionally met with in the acquired disease, which resembles impetigo in its early stages, but more closely simulates favus in its fully developed state.

The first evidence of the condition is the appearance of one or more discrete, white, "scurfy" spots on the scalp. (Fig. 10.) On minute examination a small immature indurated papule will be found. There is no congestion hyperemia, or inflammatory reaction. Gradually other similar spots appear; they cease to be discrete, and coalesce with the formation of heaped up crusts. These in turn coalesce into large patches until the whole scalp is finally involved. At this stage the patient looks as if he were wearing a tightly-fitting white cap showing a slight fringe of hair at the lower margins. (Fig. 9.) The condition is well known to the native, and goes by the name of *"wit-kop"* (white head) or *"dikwakwadi."*

The surface may be fairly smooth, or irregular from heaped-up crusting. The color is on the whole distinctly white but may rarely acquire a yellowish tinge. It is never yellow from the start. The outer layers of this crust are quite friable, but the deeper layers are firmly adherent to the scalp proper. On raising the crust no marked moisture is present, and the scalp shows the epidermis uniformly reddened, but in no way actively inflamed. In very early cases there may, however, be a slightly raised inflamed papule,

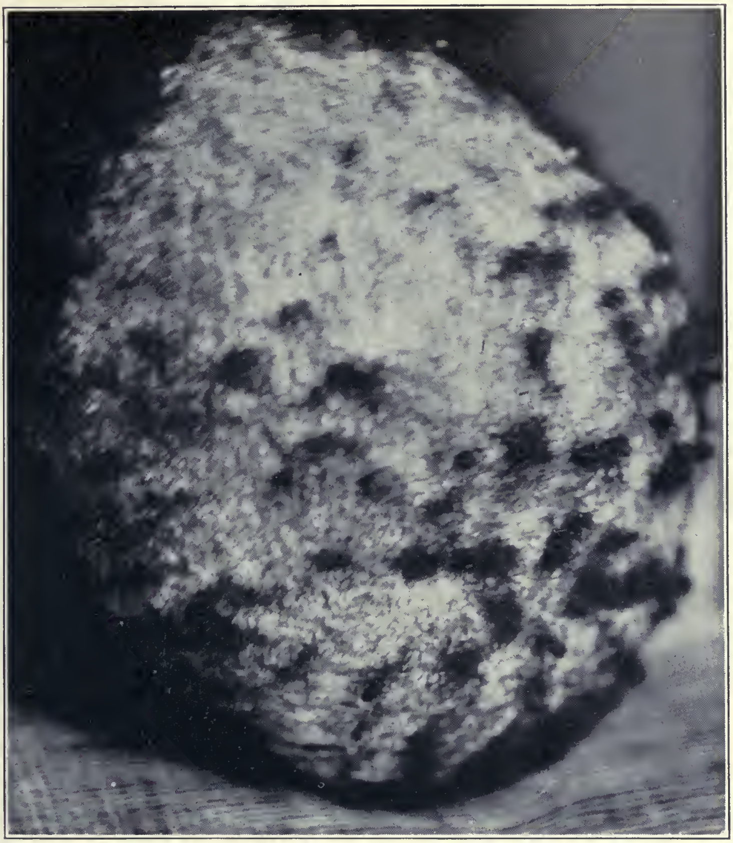


Fig. 12.—This scalp shows the regrowth of hair which is appearing in bunches or tufts among the crusts.

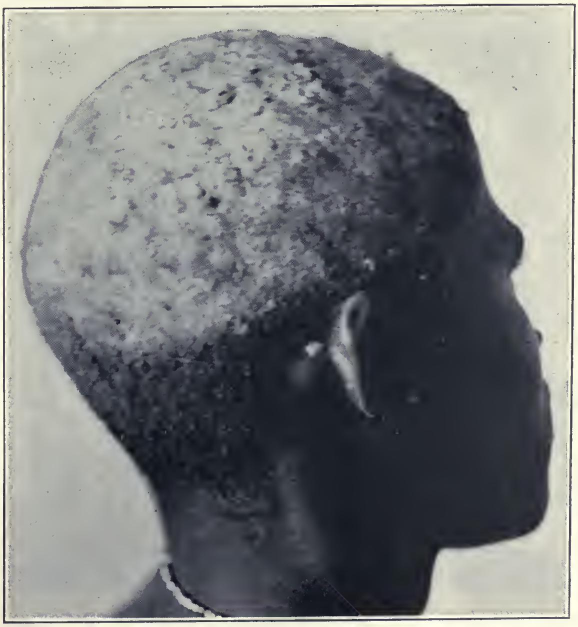


Fig. 13.—A typical case of *wit kop* before treatment. The heaping-up of crusts is well shown.

but this is not characteristic. The hair follicles are not implicated in the early stages, but later on they may become obliterated from pressure. In long-standing cases the hair will fall out in patches, but a complete regrowth of hair invariably occurs. (Figs. 11 and 12.) Cure is often difficult, but recognized antiluetic measures are generally successful. Much failure, however, has resulted from the native carrying out his mercurial treatment only spasmodically. Like most other earlier syphilitic lesions, spontaneous healing frequently takes place. At no period is there any active inflammatory process, and no local symptoms are ever caused. Thus the absolute absence of itching, heat, pain, or irritation, is characteristic and essentially typical. For this reason the native has always treated the condition with contempt and indifference.

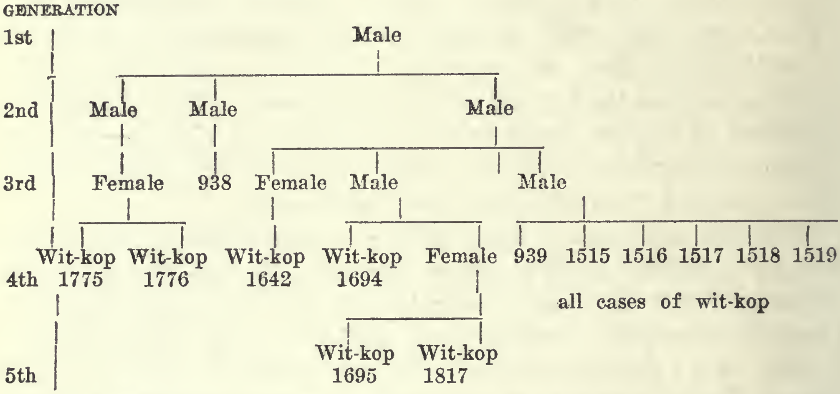
The age incidence is from infancy to late puberty, but its incidence in Bechuanaland is greatest between the ages of two and ten years. While it is seen most frequently as a manifestation of hereditary syphilis among these people, it has been known to occur as a secondary lesion in acquired syphilis. Quite recently Reith Fraser[28] had such a case under his care in the New Somerset Hospital, Cape Town.

This favoid condition is frequently associated with mucous tubercles and condylomata. One generally finds there is abnormal rhinitis present. It is not uncommon to find a congested and often petechial area around the midline of the hard palate. Accompanying this there may be some edema of the nasal mucosa. These symptoms are invariably the precursors of the severe destructive lesions of the nasopharynx so common among these peoples, and so frequently a sequela of the more chronic cases of this favoid syphilide.

In the 1009 cases placed in family groups, this condition appears in 293 cases spread over 147 family groups. Apart from the implication of the nasopharynx, 70 cases showed other active lesions which occurred before, concomitant with, or after the appearance of *"wit-kop."* Among 538 ungrouped cases *"wit-kop"* occurred in 89 cases, 18 of which showed other active lesions. So many of these cases attended for treatment so infrequently on account of the rapid clearing up of the scalp condition, that there has not been the opportunity of investigating family histories which one would have liked.

Family Tree No. 5

This family tree is presented on account of the high incidence of *"wit-kop"* among its members. These are all presumably syphilitic stock, and the families were widely scattered over the vast stretches of *Native Reserve.* There is, therefore, no question of direct contagion. The tree furnishes further presumptive evidence of the spironemal origin of *"wit-kop"*. The family groups concerned are Nos. 193 and 267. The numerals used correspond to the case numbers in the register.



In one family tree, therefore, we find ten cases of *"wit-kop"* out of eleven souls in one generation, and two cases in the next generation.

In many adult patients coming for treatment with active lesions, it is apparent that they have at some former time suffered from this condition. On being questioned, they will freely admit that such has been the case in their youth.

Like many other lesions in native syphilis this scalp condition is remarkable for its chronicity, its spontaneous cure, and the tendency to relapse in cases treated inadequately. Early cases respond to antisyphilitic measures, but the chronic cases are very obstinate. Should the condition occur during the so-called tertiary stage, like other lesions relapse is frequent, and many cases when treatment is discontinued show typical syphilitic lesions lighting into activity, at the same time as the *"wit-kop"* relapses. Cases under my care have responded to arsenobenzene, and the scalp condition has cleared up coincidently with other lesions present. (Figs. 13, 14, 15, 16.)

Case 3.—Mothscochaka, male native, age 16 years, suffered from *"wit-kop"* which involved the entire scalp to the level of the ears. It was of many years' duration. During this time mercurial and potassium iodide medication had been

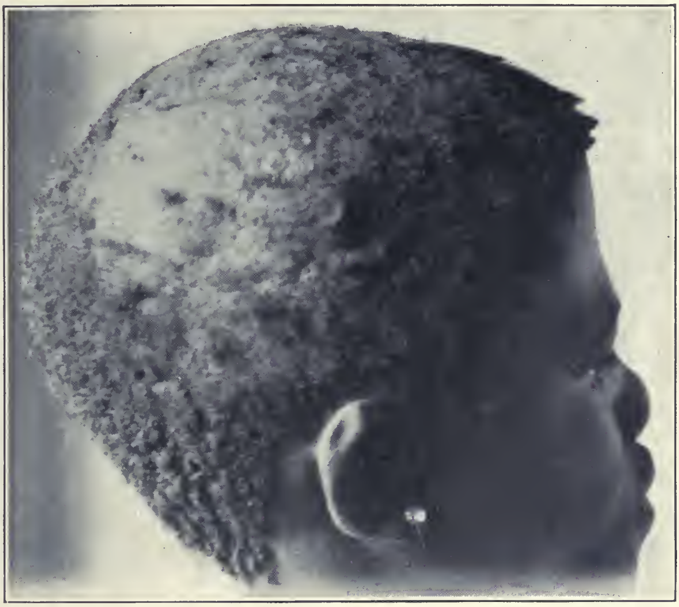


Fig. 14.—The same case as in Fig. 13, after mercurial treatment. The marked diminution in the extent of the lesion, and the new growth of hair are evident.

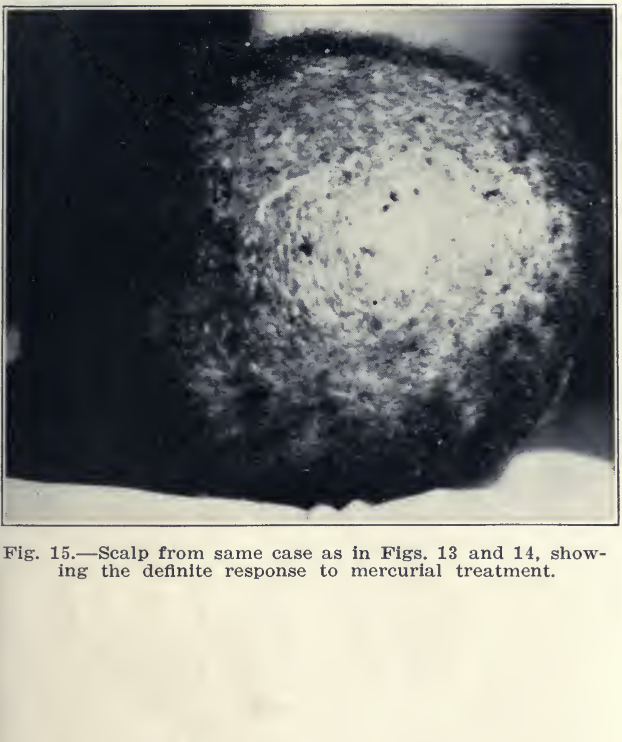


Fig. 15.—Scalp from same case as in Figs. 13 and 14, showing the definite response to mercurial treatment.

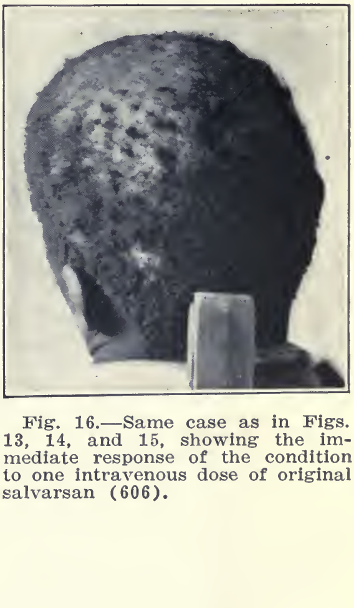


Fig. 16.—Same case as in Figs. 13, 14, and 15, showing the immediate response of the condition to one intravenous dose of original salvarsan (606).

practised, but it is uncertain how far the patient carried this out, and observation was difficult, and supervision impossible. His general condition improved, however, but a crop of petechiae on the midline of the hard palate suggested an oncoming nasopalatine necrosis. The result following the administration of 0.3 gm. salvarsan was most remarkable. The *"wit-kop"* entirely disappeared within four weeks, and there has been no recurrence. Oral mercury was continued, and the patient expressed great delight at the result.

CASE 4.—A. K., male bastard, age 25 years, had been under treatment for five years for *"wit-kop"* and pharyngeal gumma. The *"wit-kop"* had more or less cleared up, leaving the scalp completely bald. The pharyngeal gumma, however, persisted, and was accompanied by a severe breaking-down gumma of the palate, with considerable tissue destruction. Following the administration of 0.3 gm. of salvarsan the throat and palate cleared up entirely, and the remains of the *"wit-kop"* disappeared. There has been no recurrence, but oral mercury and potassium iodide have been continued.

The question naturally arises whether *"wit-kop"* is a true manifestation of syphilis or not. It seems unlikely that the syphilitic origin of the initial papule can be doubted. The development of these discrete papules is in every way similar to that of a pustular syphilide: the rapid evolution of the papule; the absence of any vesicular stage; the tendency to dry up, and the formation of crusts; the pigmented cicatrix, and the white depressed scar. From being discrete they coalesce while still in the papular stage, and then the encrustation begins. The crusts in turn coalesce into patches and the patches increase in size and coalesce until the whole scalp is involved. This is quite a typical picture of the progression of any untreated pustular syphiloderm. The crust itself is composed of masses of dried-up serum, pus cells and epidermal debris. They are white in color, but otherwise their character is constantly changing. They may be smooth and flat, and when new strata are being added from below take on the appearance of syphilitic rupia. Again they may be dry, friable, and superficial like favus, or soft and wafer-like as in impetigo. True tough, thick, and adherent syphilitic crusting is also frequently seen.

Additional evidence of the luetic origin of the condition is seen in the mass of family histories, the continual combination and association with undisputed syphilitic lesions, the results of antisyphilitic treatment, and a positive Wassermann reaction. In addition one must not ignore the fact that this scalp condition has not yet been seen in a nonsyphilitic patient. Moreover in every case it responds to treatment in exactly the same way and at the same rate as other concomitant lesions.

To assume that the condition is due to some cause other than the *Spironema pallidum* one would look for evidence of widespread contagion. Were it due to some spore growth, this would undoubtedly be so. The native in his kraal, where living space is limited, and where large families are crowded together, would offer an ideal hunting ground for the spread of such an infection. Old and young would be infected alike, and it would tax the ingenuity of any public health administration to devise methods of curtailing its spread. Yet one finds that it crops up in the districts quite irregularly, and one kraal may house several patients suffering from *"wit-kop"* while adjacent kraals are free of it. In addition it should be noted that Europeans following trades and other occupations in native reserves full of hundreds of such cases never, by any chance, become infected.

Yet the suggestion that this scalp condition is due to causes other than the *Spironema pallidum* has been put forward seriously. Mitchell and Robertson[29] demonstrated a fungus from the cases Nos. 882 (family group 135), 1246 (family group 44), 1647 (family group 191), and 1211 (ungrouped). The first case gave a negative Wassermann reaction, but the three others were positive.

It may be of interest to quote these workers' description of the fungus which they demonstrated: "Vertical sections of portions of the infected scalp showed on the surface a honeycomb mass composed of pus cells, epithelial debris, blood corpuscles, and oval or rather cuboid dark staining bodies (conidia) bound together by a fine filamentous network of threads of a branching fungus. These filaments and conidia can be seen in sections invading the hair follicles (Figs. 17 and 18), which they often completely block up; they also in many cases involve the hair itself. The conidia are large nucleated cells, cuboid in shape, frequently collected in masses, but sometimes apparently springing from the terminal portions of the large branching mycelial filaments. Numerous cultures were made from the crust and from the deeper parts of the affected scalps; from the majority of the tubes it was possible to isolate a fungus which grew slowly at ordinary room temperature upon glycerine agar and Sabouraud's media. If the medium be moist, the growth at first looks like a luxuriant crop of coliform

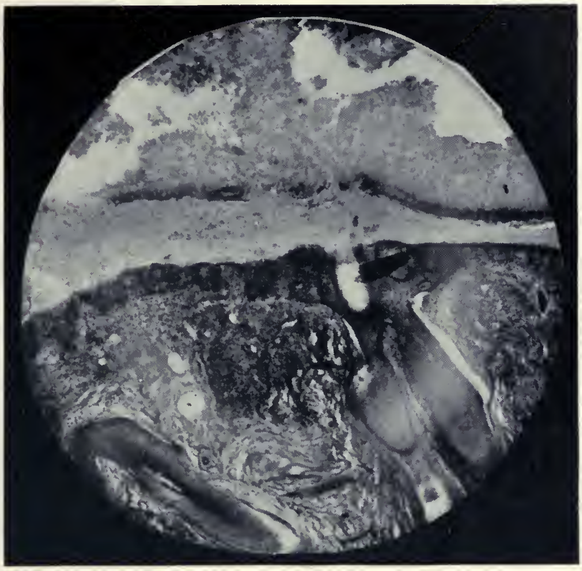


Fig. 17.—Vertical section of portion of scalp from case of *wit kop,* showing on the surface a honeycomb mass, made up of pus cells, epithelium, and debris. (Low power.)

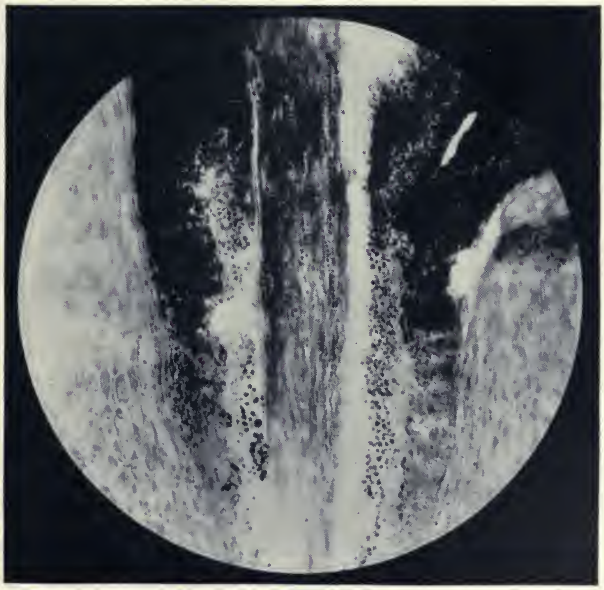


Fig. 18.—Vertical section of portion of scalp from case of *wit kop* showing cuboid dark-staining bodies (conidia ?), and a fine filamentous network of a branching fungus (Mitchell and Robertson) invading the hair follicle and the hair itself. (High power.)

colonies etched with very fine wavy lines. After 10 to 12 days, fine, snow-white filaments can be noticed arising from the central part of the growth. As the medium dries, the whole surface of the growth becomes coarse, corrugated and white, as if dusted with fine lime.''

These workers go on to say that ordinary white mice when placed in contact with this fungus growth develop an intense itching, with the appearance of minute papules in 8 to 10 days. The itching is so intense that several of the mice scratched their ears right off. Large crusts never formed, but a greyish-white powdery dust could be noticed round the edge of the lesion. The fungus was readily recovered from the infected mice. The fungus is stated to appear to be closely allied to the *Achorion Schönleini* of favus. Cultures of *Sarcina lutea* were also isolated from one of the cases.

The following histories of the cases in which Mitchell and Robertson demonstrated their fungus may be of interest:

CASE 5.—Caorewe Ramotho, No. 1211 (ungrouped) had been under mercurial and potassium iodide treatment for four years. It is exceedingly doubtful if treatment was persevered with, for the patient spends his time begging about the stores. His father is dead, and no luetic family history could be obtained. Wassermann reaction positive.

CASE 6.—Kebiledewan, No. 882, family group No. 135 (*vide* family tree No. 4), male native, under 14 years of age, had been under mercurial treatment for precisely five years. This was very irregular, however, for he was a cattle herder and spent most of his time on the veld. Wassermann reaction negative.

CASE 7.—Jasopo Maeco, No. 1647, family group No. 191, male native, over 14 years of age, had been under treatment with mercury and potassium iodide for 18 months. He also was a cattle herder, but his syphilitic condition had shown considerable improvement. He is the brother of Nos. 935 and 936 who were discovered to be suffering from syphilis four years previously. Wassermann reaction positive.

CASE 8.—Mamoto-kane, No. 1246, family group No. 44, female native, under 14 years of age, had been receiving mercury and potassium iodide for three years and ten months, but had been very neglectful and irregular in her attendance. For a short time regular treatment had been maintained with resulting improvement, but later even irregular attendance could only be secured under intimidation. Wassermann reaction positive.

While it is interesting to note that this fungus flourishes in the scalps of these cases, it cannot be seriously considered as evidence likely to alter one's conception of the syphilitic origin of the lesions. Similar errors have been made many times in the History of Medicine, and one need only recall the fungus demonstrated by Powell in 1896 and heralded as the cause of yaws. The attribution of a fungus as the causal factor in *"wit-kop"* is a case in point, where one might be led astray by the temptation to jump to conclusions. Apart altogether from the circumstantial evidence furnished by so small a number of cases as Mitchell and Robertson had at their disposal, it is interesting to observe the effect of this fungus on mice. The intense irritation and inflammation caused the victim to scratch so hard that his ears were rubbed off. Yet in the human subject the most characteristic feature is the absolute absence of irritation, heat, itching and discomfort.

It would seem, then, that the condition is a papular syphiloderm characteristic of the Bechuanaland native. When the lesion is fully developed, a spore growth is apparently established in some cases, but it is not clear that this has any pathologic significance, or that it influences in any way the development or evolution of the condition. If the fungus described were allied to the causal fungus of favus, it is reasonable to contend that *"wit-kop"* would be as contagious as that disease. We have ample evidence, however, that it is not. The ease with which mice were infected, and the failure to reproduce an encrusted lesion are significant.

SUMMARY

This contribution deals with a study of syphilis in the Bechuanaland native. An abstract of the family histories of 1009 cases is presented, and observations accruing from 538 cases which do not fall into family groups.

The possible methods of transmission of syphilis are summarized, with special reference to conditions obtaining in Bechuanaland. The unique syphilization of families on a large scale is noted.

The question of whether the disease is syphilis or frambesia tropica is dealt with. The evidence that it is syphilis is conclusive.

Evidence is had which suggests strongly the possibility of the transmission of syphilis to the third and subsequent generations.

Variations in symptomatology between European syphilis and that seen in the Bechuanaland native are discussed. Most attention is given to (1) the absence of visceral lesions, (2) the apparent insusceptibility of the cerebrospinal axis to attack, (3) the high incidence of *syphilis hereditaria tarda,* (4) the marked chronicity and slow development of isolated lesions, and (5) the clinical characteristics of a prevalent favoid condition of the scalp locally known as *"wit-kop."* In this connection some account is given of a fungus described as a possible causative agent.

CONCLUSIONS

It will be seen that hereditary syphilis is by far the most frequent type of this disease met with in Bechuanaland. Acquired syphilis occurs, but is comparatively rare. The chancre is seldom seen, and as often as not is extragenital. It would seem reasonable to suggest that a combination of syphilis d'Emblée and syphilis insontium may be responsible for the manner of spread of much of what acquired syphilis occurs in these regions. The contagion of heredosyphilis is, in view of the widespread incidence of this condition, a factor of some importance as far as it affects nonsyphilitic natives and strangers, particularly when the mode of life and habits of the native are considered.

There is much presumptive evidence that the possibility of hereditary transmission to the third generation is a very real thing. The rarity of acquired infection is an important point in deciding the issue, together with the very widespread syphilization of whole families which one meets.

The absence of visceral syphilis capable of producing clinical signs is noteworthy. It is accounted for chiefly as a racial peculiarity, possibly resulting from the untaxed state of his digestive apparatus, his slow rate of metabolism, and the strain-excluding, easy-going, open air existence which he leads.

The prevalence of a specific pulmonary fibrosis is not so great as has been suggested by other workers in other parts of South Africa. Brock[23] concluded that 80 per cent of the natives show a fibroid condition of the lungs, or an indurated enlargement of the epitrochlear gland, or both, and that syphilis is responsible for both of these conditions. One considers that epitrochlear adenopathy is suggestive of spironemal infection, but taken alone is quite inadequate evidence on which to base a diagnosis. In laying a pulmonary fibrosis in 35 per cent of natives to the charge of syphilis, particularly among natives engaging in work in the dust-laden air of the Rand Gold Mines, one is of the opinion that his figures greatly exaggerate the position.

The absence of neurosyphilides among colored races has frequently been recorded. This phenomenon is observed in Bechuanaland. The fact that the native's cerebrospinal axis is not submitted to the strain and worry of modern civilization may be part of the explanation. Much more important seems to be the antibody supply which he receives from his general systemic circulation which is constant and prolonged over an indefinite period. This antibody supply is at hand when any spironemata are advancing to the attack, and clinical signs fail to supervene. The treatment of all these cases consisted of oral mercury in moderate doses, and potassium iodide, over very long periods. Mercury, as we know, stimulates antibody production in small doses—while it inhibits this production when administered in large doses—and this may be a further part of the explanation.

The very high incidence of *syphilis hereditaria tarda* is particularly striking. It is accompanied by a very small incidence of abortions and miscarriages, and a low infant mortality. Whether this occurs most frequently in second, third, or subsequent generations of heredosyphilis, or in generations where there may be a normal individual, an acquired syphilitic, or a heredosyphilitic on either side of the previous generation, is quite uncertain.

The typical chronic and comparatively nondestructive course of isolated lesions is characteristic of native syphilitic disease met with in Bechuanaland, but particularly so of *syphilis hereditaria tarda.*

"Wit-kop," a favoid condition of the scalp is characteristic of heredosyphilis in Bechuanaland, but it has also occurred coincident with the secondary eruption in native acquired syphilis elsewhere. It has not yet been met with in a European or in a native nonsyphilitic. A fungus which apparently flourishes on scalps so affected has been suggested as the causal factor. The overwhelming bulk of evidence, however, goes to indicate that *"wit-kop"* is spironemal in origin.

It is a pleasure to have this opportunity of acknowledging the encouragement and practical assistance I have received in this work from Sir Edward N. Thornton during the years when his departmental activities brought him to Bechuanaland. My thanks are also due to Dr. A. Reith Fraser, Cape Town, for his generous assistance and numerous suggestions in the preparation of this paper.

I am also indebted to the Health Department, Union Government of South Africa, for permission to use Figs. 9, 11, 17, and 18.

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THE USE OF SODIUM THIOSULPHATE IN THE TREATMENT OF POSTARSPHENAMINE DERMATITIS EXFOLIATIVA; REPORT OF A CASE

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IN a comprehensive review of the accidents following arsenic therapy for syphilis, Moore and Keidel[2] have summarized the various theories for their occurrence as follows: (1) damage to the hematopoietic system; (2) the cumulative effects of arsenic; (3) damage to the liver; and (4) anaphylaxis. Stokes and Cathcart[4] have stressed the apparent relation of chronic focal and intercurrent infections to postarsphenamine dermatitis, and proposed the highly plausible theory of allergic instability produced by colloidal changes due to the use of arsphenamine and to acute or chronic bacterial infection with resultant protein sensitization.

The prodromata of severe cutaneous reactions following arsenic treatment are nervousness and irritability, gastrointestinal upsets, evidence of acute infection, which may or may not be present, fever after intravenous medication, and itching of the palms and soles.

The symmetrical, acute, maculopapular or vesicular dermatitis with great edema, intense itching and burning, and rapidly mounting temperature soon appears. Diarrhea may be severe, the foul-smelling stools resembling those of pellagra. Exfoliation of fine and large flakes occurs, and casts of the foot or hand may be formed as in erythema scarletinoides and scarlet fever. The extreme tenderness of the skin, together with the tense edema, makes venipuncture difficult.

The active treatment of the severe cutaneous accidents following the use of arsenicals was formerly symptomatic. Once the metal was injected, it could not be recovered. Thanks to the work of Ravaut[3] of France, and McBride and Dennie[1] of this country, arsenic and other heavy metals can be precipitated into insoluble compounds by the intravenous injection of sterile solutions of pure sodium hyposulphite as follows:

First day	0.15 in 10 c.c. of water
Second day	0.3 in 10 c.c. of water
Third day	0.45 in 10 c.c. of water
Fourth day	0.6 in 10 or 15 c.c. of water
Fifth day	0.75 in 15 or 20 c.c. of water
Sixth day	0.9 in 15 or 20 c.c. of water
Seventh day	1.0 in 20 c.c. of water

and in doses of 1 gm. each day thereafter, as indicated. If introduction by vein is impossible, oral and rectal administration of the compound should be used and may lessen the edema enough to make venipuncture possible. These routes are poor substitutes, however, as a rule.

The following case is of interest because of the normal hepatic function throughout its course, the rather high retention of blood chloride, and the prompt response to graduated intravenous injections of sodium hyposulphite.

CASE 13831, Mrs. A. J. L., thirty-five years of age, came to the Clinic in July, 1922, because of pain in the chest and loss of weight. She had been married eight years and had had one normal delivery followed by five miscarriages. Six months before, she had had a severe attack of influenza, followed on recovery, by the present symptoms. She had been told that she had tuberculosis of the lungs and had received about twenty-five hypodermics of ''arsenic'' from her family physician in the six months preceding admission to the Clinic.

Physical examination revealed a tall, pallid, undernourished woman of middle age. Her hair was dry and lustreless, and there was a pronounced tendency towards ichthyosis throughout the cutaneous areas. There was rather marked general glandular enlargement, and periosteal thickening of both tibiae. There were no signs of chronic infection of the teeth, nose or accessory sinuses, but some pus could be expressed from the right tonsil. The only abnormal findings in the lungs were fine, moist rales over the right upper lobe which disappeared on coughing. Stereoscopic films showed only a slight increase in both hila shadows. Physical examination was otherwise negative. A serum-Wassermann test was strongly positive but the urine, blood nitrogen and spinal fluid examinations were entirely negative. A blood count revealed erythrocytes 4,200,000, leukocytes 6,000, and hemoglobin 55 per cent. The differential count showed polymorphonuclears 75 per cent, lymphocytes 24 per cent, eosinophils, none, transitionals 1 per cent.

The patient was put on a rather high carbohydrate diet, and between August 12 and September 18, a total of 2.6 gms. of neoarsphenamine and 0.3 gm. of soluble mercury was given. She gained in weight and felt stronger, but twenty-four hours after her fourth in-

COMPLETE STUDY OF THE BLOOD, WITH THERAPEUTIC AND CLINICAL NOTES

DATE	RED CELLS	HEMO-GLOBIN	DIFFERENTIAL COUNT						BLOOD CLOTTING TIME	REMARKS
			WHITE CELLS	POLYS	SMALL LYMPH	LARGE LYMPH	EOSIN	TRANS		
7/30	4,200,000	55%	6,000	75%	20%	4%	0	1%	.43	Hepatic function* normal. Basal metabolic rate +2.43
9/20	4,200,000	50%	6,400	76%	22%	3%	0	1%	.57	Two days after onset of symptoms.
9/24	4,300,000	52%	5,900	75%	20%	5%	0	0		
9/30	4,800,000	48%	5,100	70%	18%	2%	10%	0		
10/8	5,000,000	65%	5,200	51%	22%	8%	18%	1%		Patient delirious
10/16	5,100,000	70%	4,200	60%	14%	2%	23%	1%		Temperature high
10/18	4,800,000	65%	5,430	50%	10%	10%	28%	2%		
10/22	4,900,000	76%	5,300	40%	12%	3%	41%	2%		
10/24			5,300	58%	14%	5%	22%	0	.95	Sodium hyposulphite in daily doses intravenously
10/26	4,790,000	73%	5,600	51%	20%	7%	26%	0		
10/28			6,100	67%	14%	6%	16%	0	1.61	Hepatic function normal
10/29	4,300,000	59%	5,800	81%	15%	3%	0	0		Metabolic rate +9.84
10/30	4,400,000		5,200	80%	18%	2%	0	0	.95	Dismissed from hospital
11/2	4,300,000	59%	6,320	82%	13%	5%	0		.53	Hepatic function normal Metabolic rate +3.56
12/12	4,800,000	78%	5,400	80%	20%	0	0		.58	Apparently recovered

*Hepatic function test used was the levulose sugar tolerance test, applied in the same manner as the glucose tolerance test.

jection of neoarsphenamine she became suddenly nauseated and complained of intense general itching, pain in the abdomen, and swelling of the tongue. Epinephrin and a drastic cathartic were given but on the following day a generalized vesicular dermatitis with marked edema appeared, accompanied by clouding of consciousness, loss of the knee jerks, and contraction of the pupils. The temperature rose steadily, and the edema increased until venipuncture became impossible. With decrease of the mental symptoms a salt-free and low-protein diet, and administration of sodium hyposulphite by rectal tap were instituted. On October 22, when the edema had somewhat decreased, injections into the veins of graduated doses of sodium hyposulphite were given daily until one gram was administered each day. Recovery was rapid, although the exfoliation of large flakes continued up to the time of dismissal from the hospital. A chart showing the complete blood findings and notes on the patient's condition is appended. The urine consistently contained large traces of albumin and was of rather high specific gravity. The persistently normal hepatic function curves are of interest if it is held that the levulose sugar tolerance test is of value.

The value of the routine removal of foci of infection before antisyphilitic treatment is instituted would seem to be illustrated by this case. Allergic instability is suggested by the occurrence of the reaction after the fourth injection of neoarsphenamine, the small amount of the drug employed, and the eosinophilia with gastrointestinal symptoms.

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THE COMPARATIVE VALUE OF KOLMER'S NEW ANTIGEN IN THE ROUTINE WASSERMANN TEST*

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THE requirements for a practical and reliable Wassermann test in routine work are of the strictest sort. Where the Wassermann reaction is done routinely on all cases of a chronic nature coming up for diagnosis it must be depended upon to show a clear-cut reaction without being liable to confusing false positives. A Wassermann test giving results which one must be continually explaining is a source of confusion. A test which misses a considerable per cent of clinical syphilis, or one which gives frequent weakly-positive reactions unsupported clinically is often more annoying than helpful. Obviously little dependence can be placed on a Wassermann test in the obscure case, where it is most needed, if it gives false reactions, either positive or negative, in a fair proportion of clear-cut clinical cases.

In the very nature of the Wassermann test the main source of question lies in the antigen. Heretofore where a single antigen has been used one has been faced with the proposition of using one of low sensitiveness where avoidance of false positives was more desirable than catching all cases of syphilis or of employing a highly sensitive antigen when false positives were considered less important than false negatives. In the attempt to reduce both undesirables to the minimum there appeared the custom of using two or more antigens of different degrees of sensitiveness. In interpreting the reading of such a Wassermann test if there was disagreement between or among the antigens it has been customary to average the results obtained, thus producing a fairly high proportion of weak positives without, in a manner, solving the difficulty at all. Obviously if two antigens are used and one gives a negative reaction while the other is positive one or the other is wrong and to average the results of the two is simply to beg the question, take both as correct, and report it in weak and uncertain terms. To take the extremes of delicacy in antigens, the plain alcoholic organ

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extract and the cholesterolized alcoholic extract, it is not far wide of the mark to say that a negative reaction with the former or a positive test with the latter may mean nothing at all. The plain alcoholic organ extract, while highly dependable when giving a positive reaction, will fail in a considerable per cent of cases of syphilis. A cholesterolized alcoholic extract is so productive of false positives that in my opinion it should never be used in a diagnostic Wassermann test alone. In the midground between these two comes the acetone insoluble lipoids of heart muscle. Frequently one obtains an excellent antigen of this preparation, but not infrequently one which is unreliable or low in antigenic quality is the result of the same extraction.

To overcome the manifest difficulties heretofore encountered with one or more of these antigens in common use Kolmer, after an exhaustive study, has introduced an antigen which in his hands appears to have reduced the false positives and to give much more dependable results.

The purpose of this paper is to compare the results obtained from the three antigen Wassermann test (alcoholic organ extract, acetone insoluble lipoids and cholesterolized alcoholic extract) in a series of routine tests with a similar series in which only the new Kolmer antigen was run. Both series were run with the antisheep hemolytic system in water-bath fixation, the only difference in the two series being in the antigen.

In the three antigen series are 976 tests and in the one antigen series are 1,190 tests. In the former ± and + reactions were distributed as follows: alcoholic extract 27 or 2.7 per cent; acetone insoluble lipoids 28 or 2.8 per cent; cholesterolized alcoholic extract 25 or 2.5 per cent; while a composite reading of the three gave 121 or 12.2 per cent. In other words 12.2 per cent of the series had a Wassermann test reading which was doubtful in interpretation and consequently often confusing. ++ reactions were distributed as follows: alcoholic extract 7 or 0.8 per cent; acetone insoluble lipoids 14 or 1.4 per cent; cholesterolized alcoholic extract 22 or 2.2 per cent; while a composite reading of the three gave 13 or 1.3 per cent. +++ reactions occurred as follows: alcoholic extract 3; acetone insoluble lipoids 2; cholesterolized alcoholic extract 31 ar 3.1 per cent; composite reading 8 or 0.8 per cent. ++++ reactions were distributed as follows: alcoholic extract 26 or 2.6 per cent; acetone insoluble lipoids 28 or 2.8 per cent; cholesterolized alcoholic extract 91 or 9.1 per cent; composite reading 24 or 2.4 per cent. If ++ or better are considered as positive readings a composite reading of the three gives 45 or 4.5 per cent positive Wassermanns for the series.

In the series of 1,190 cases in which only the Kolmer antigen was used ± and + reactions occurred in 23 or 1.9 per cent; ++ reactions were obtained in 7 or 0.5 per cent; and ++++ reactions occurred in 34 or 2.8 per cent. Considering ++ or better as positive there are 41 or 3.4 per cent.

Comparing the two series we find that with the three antigen test there occurred 12.2 per cent doubtful reactions while with the Kolmer antigen alone there were only 1.9 per cent. Of weak positives there were 2.1 per cent in the former against 0.5 per cent in the latter. Of ++++ positives 2.4 per cent were obtained in the former against 2.8 per cent in the latter, while ++ or better reactions indicated syphilis in 4.5 per cent of the former against 3.4 per cent in the latter.

Critical analysis of these comparisons cannot fail to favor the Kolmer antigen. Confusing doubtful reactions are markedly reduced, weak-positives are cut to a fourth the number, and yet not at a sacrifice since ++++ positive reactions were obtained in even a higher per cent. It appears that both dependability and specificity, if the word may be used, are improved.

Even the comparison of these percentages fails to carry the difference in satisfaction encountered in working with the two methods. With the three antigen methods there was the continually repeated question of the result of the test; in 12 per cent or more there was an explanation of the result to be made and usually the test to repeat, possibly several times, while the interpretation of the result was often a matter of a compromise among three different readings or two against one. With the new antigen an explanation and a repeated test is seldom in order and our report is of far more value and satisfaction to the clinician.

In addition there is the advantage in simplicity and the saving of time, labor and supplies. The antigen which was used in this series was prepared exactly as specified by Kolmer[1] and is antigenic in less than 0.1 c.c. of 1:200 dilution and anticomplementary in 1 c.c. of 1:10 dilution, properties which are remarkable when compared to the antigens of other composition in common use. It appears that different extracts are fairly uniform in these desirable properties whereas the qualities of other antigens are widely variable. Of course herein lies the explanation of its dependability—its high antigenic and low anticomplementary properties.

Incidentally it is of interest to note the incidence of the positive Wassermann in this series of cases which takes in only private patients of the upper social level. Taking the latter series of 1.190 patients, 3.4 per cent had a positive Wassermann reading. This will tally very closely with our final clinical diagnosis and is apparently a good index of the incidence of syphilis in a medical clientele of the better sort suffering from chronic disease in this section.

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VALUABLE SUGGESTIONS FOR CONTRIBUTORS TO THE AMERICAN JOURNAL OF SYPHILIS

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Let your phraseology express one meaning and one only. Be clear.[2]

Manuscript.—Manuscripts should be typewritten, with wide margins, and double spaced, on one side of paper 8½ by 11 inches in size. The original copy should be sent to the "Journal" and the carbon copy retained by the author. Number the leaves consecutively, beginning with the title page. Put your name and address on the manuscript.

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Arrangement.—As authors are quoted in the text give each a number in the order of citation, and number the bibliographic reference with the same number. Arrange the references in a list at the end of the article in the order of the numbers (see below), or arrange items in alphabetical order according to last names of authors, and distinguish between articles by the same author by the use of the date after his name in the text.

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Original Articles

DIAGNOSIS AND TREATMENT OF SYPHILIS OF THE NERVOUS SYSTEM*

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THE subject of neurosyphilis belongs to the everyday practice of neurologists, and the following remarks are intended to give the known facts in the diagnosis and treatment rather than the etiology and pathology of the disease.

The question is often asked: "What is the percentage of neurosyphilis as compared with nonspecific cases?" The answer varies with the location of one's practice. In my service at Cook County Hospital I could easily figure out sixty-five per cent neurosyphilis in the nervous wards, while in my private practice the percentage falls as low as ten per cent. The figures become somewhat higher in outside consultation practice. The fact remains that a large number of neurologic cases—especially the organic diseases—are caused by syphilis.

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*Lecture delivered before the Englewood Branch of the Chicago Medical Society.

The subject of neurosyphilis is so extensive that I know not where to begin nor where to end. Some of our medical friends have long been under the impression that a serologic examination was the only thing needful, and that the latter saves one the trouble of making a clinical diagnosis from symptoms. Nothing is further from the truth, and most physicians have been disillusioned on that score. A clinical diagnosis of neurosyphilis is quite as important today as it ever was; indeed, it is even more important than the laboratory diagnosis which is often negative or doubtful when the clinical findings are definitely positive. Any one who makes a diagnosis of neurosyphilis,—tabes or cerebral syphilis,—from a Wassermann only, thereby proves that he knows nothing of clinical medicine.

In the examination of every patient careful search is made for evidence of organic disease, which includes specific disease. The routine examination of reflexes, deep and superficial, of the pupils, motility, and sensation, almost always leads to a correct diagnosis. There are certain differences between nonspecific organic nervous disease and that caused by syphilis. For instance, take the case of hemiplegia—paralysis of face, arm, and leg of one side. While apparently there are no differences observable between one case and another, to the trained observer there are many such. These are exceedingly helpful and enable one to make the diagnosis before a Wassermann has been made, and sometimes in the face of a negative Wassermann finding. I shall recur to this subject a little later.

Meanwhile it may be well to call your attention to the newer classification of syphilis of the nervous system into (a) interstitial and (b) parenchymatous neurosyphilis.

(a) What is interstitial neurosyphilis? This is the type in which the interstitial tissues—the connective tissue, blood vessels, the membranes and the glia—are primarily affected, while the parenchyma may be secondarily involved. The spirochetes have, by means of the blood stream and lymph current, been carried directly to those tissues and have there caused inflammatory changes. It is exceedingly important to remember this difference and that the interstitial type of neurosyphilis has the most favorable prognosis and responds readily to mercury and salvarsan.

(b) What is parenchymatous syphilis? It is that form of neurosyphilis in which there are no more present *inflammatory* conditions, but the *parenchyma* itself has become affected; the nerve cells and nerve fibers have *degenerated.* As in the preceding variety—the interstitial type—the spirochetes have invaded the tissues and have done destructive work, only here we find true degeneration in the nerve tissues proper, while in the former the parenchyma is still intact. The nomenclature is similar to that employed in the classification of kidney lesions. Knowing how difficult it is to chase after the spirochetes once they have left the blood stream and settled permanently in the parenchyma of the nervous system, one realizes the seriousness of the prognosis. It is only by ignoring the true condition as it exists in parenchymatous neurosyphilis that we can entertain the fond illusion that antispirochetal remedies can reach the source of the disease.

Examples of parenchymatous neurosyphilis are tabes and general paresis; in the one the cord parenchyma, notably the posterior columns and its extensions up and down the cord, is in a process of degeneration, while in general paresis the cortical cells and tangential fibers are undergoing progressive degeneration. Though the prognosis in this form of neurosyphilis is grave, yet the possibility for therapeutic interference is given in the fact that the degenerative process is rather slow, taking in the tissues gradually. Some of the tissues can be saved when treated early and in a modified way, as will be described later.

To return to *clinical diagnosis;* there are a few practical points which may be helpful in most cases. One of the important points to remember is, that syphilis produces lesions in the nervous system that are just a little different from those caused by other etiologic factors. Take for instance hemiplegia, a subject on which I have already touched. It is true that the hemiplegic picture in itself is the end-result of one of several causes. Usually apoplexy precedes the development of paralysis of one half of the body, but apoplexy itself is only a general term for a more or less sudden development of loss of power in one or more extremities, accompanied or not by loss of consciousness. Cerebral apoplexy may be caused by hemorrhage, embolism, or thrombosis of cerebral vessels.

In apoplexy from *hemorrhage* symptoms appear suddenly—the patient loses consciousness, develops stertorous breathing, slow pulse, deep respiration; and unilateral paralysis remains when consciousness returns. The antecedents are usually high blood pressure, a certain age (between 45 and 60 years) and physical or mental strain incident to certain occupations. The reason for the suddenness of onset is to be sought in the fact that the artery of hemorrhage (the lenticulostriate artery of Charcot) gives way and permits the heart to pump blood into the brain through the torn vessel at the rate of from 60 to 80 times per minute. Of course, the pressure from this additional amount of blood is sufficient to disorganize all forms of brain function temporarily and to damage the internal capsule—the motor tract—more or less permanently. This picture at the onset differs entirely from that of apoplexy caused by embolism and thrombosis.

In *embolism* the onset is also sudden, but the patient is usually younger and the subject of a cardiac lesion sufficiently severe to enable emboli to reach the cerebral circulation; only occasionally may an embolus be derived from an aortic aneurism. Patients suffering from embolic apoplexy do not lose consciousness during the attack, but the attack appears as suddenly as in hemorrhagic apoplexy.

Thrombotic apoplexy is characterized by slow onset of hemiplegia and possibly of aphasia, without loss of consciousness in the majority of cases. In this variety the patient loses the use of arm, leg, and often of speech, because his arteries become plugged by clotting within them. The reason for the slow development of paralytic symptoms—from minutes to days—is to be found in the phenomenon of clotting, which requires time for its completion. Thus is explained the incomplete hemiplegia which often precedes the complete paralysis. As certain conditions are required before clotting can take place in a living artery, these must be looked for. Low blood pressure (slow blood stream) and roughness of the arterial coat are requisites for thrombosis. These conditions are given in the artery of old age (after 65) and the majority of patients suffering from the effects of apoplexy due to thrombosis are old persons, except one group of patients, the syphilitics, in whom the thrombosis is the result of *specific* endarteritis.

This preliminary digression into the etiology of apoplexy was necessary to bring out a differential diagnostic point of great importance.

When called to see a young individual of from 20 to 40 years, suffering from apoplexy, we examine the cardiovascular system for evidences of valvular lesion and aneurism, familial arteriosclerosis and kidney disease. If we are informed that the attack was rather slow in onset and that the patient had suffered from nocturnal headaches days and weeks prior to the attack, but which cephalalgias subsided entirely or in part after the onset of a hemiplegia, we are on the trail of a diagnosis of neurosyphilis of the interstitial variety. Instead of nocturnal headaches some patients suffer from a state of somnolence amounting to stupor for days and weeks prior to the onset of hemiplegia. This particular *grouping* of symptoms is a great aid in the diagnosis of syphilis. In such a case the hemiplegia may not follow the classical rules as laid down in the texts. For instance, a rightsided hemiplegia may be unaccompanied by aphasia, or it may be incomplete.

Syphilis appears entirely ''anarchistic'' in its tendencies; it does not follow rules at all. From all sources we learn that the most typical thing about syphilis of the nervous system is, that it is not typical at all; it is mostly atypical. Not only may the patient not be suffering from an aphasia when he should, but instead of the arm being most affected and the leg and face least, it is the reverse in his case. In other words, there is mostly a certain something about the disease picture which does not correspond to the classical appearance of the disease when produced by other causes.

Finding this atypical grouping of symptoms enables one to call attention to the probable existence of syphilis and justifies the placing of the patient on vigorous antisyphilitic treatment even before the laboratory has reported. There is no time to lose in such cases and one may be far from a reliable laboratory, or the laboratory may have given a doubtful or negative Wassermann report. The fact must not be forgotten that vascular syphilis may give a negative Wassermann, because the syphilitic process is localized in the vessel wall and may have little or no communication with the blood stream.

Possibly I have dwelt too long on this portion of interstitial syphilis; its frequency is my excuse. There is another type of interstitial neurosyphilis which is more readily recognized. I refer to the case in which headache is the sole manifestation of the disorder, or in which "fits" occur suddenly, or there may be both. The sufferer is from 25 to 35 years old, and insists that he never before had convulsions. He loses consciousness, foams at the mouth, but is not sleepy after the attack. The latter differs from ordinary epilepsy in that it is followed by severe headaches, or the headaches may persist during the intervals between attacks. Again there is a difference between these convulsions and classical epilepsy; it is atypical epilepsy. In the case under discussion, both the fit and the headache are probably caused by localized infiltration of the meninges. It should not be treated as an ordinary case of epilepsy, but thorough investigation should be made for syphilis and proper treatment instituted both for the disease and for the symptoms of the disease.

In speaking of meningitis, the syphilitic form of meningitis is unlike any other form. We know tubercular, influenzal, and pneumococcic meningitis, as well as the epidemic variety. All are generalized types except the syphilitic variety, which usually is *localized.* There may be some infiltration of the meninges with gummatous material anywhere at the base or cortex, preferably at the base. A favorite location is the interpeduncular space with its third nerve issuing from it; hence the frequency of third nerve lesions in neurosyphilis. Another favorite spot is the region of the optic chiasm, giving rise to the various visual disorders, including syphilitic optic neuritis and hemianopsia. The fourth and sixth nerves may likewise be involved, because of infiltration at the base of the brain. Indeed, the patient may come to us with slight drooping of the eyelids, or ptosis, because of diplopia. There may also be some drooping of one side of the face—facial palsy—with or without weakness of the same or the opposite arm and leg. Another case may present a slight degree of aphasia, motor or sensory, or mixed. When the bulbar region is involved, there may be dysarthria and hypoglossal nerve disorder, manifested by atrophy and deviation of the tongue towards the paralyzed side. One or more nerves at the base of the brain may be implicated in the syphilitic process, which will become manifest by corresponding symptoms. In almost all these patients close examination will reveal a difference in the size of the pupil, or the typical or atypical Argyll-Robertson pupil may be in evidence; occasionally the pupil may be fixed or rigid to both light and convergence. Syphilitic localized meningitis at the base is known by its tendency to appear in spots indiscriminately and is not limited to one side of the brain. Whenever, therefore, we find disorder of several cranial nerves peculiarly distributed, one or more nerves on one or both sides, the diagnosis of neurosyphilis can safely be made. Diffuse lesions at the base of the brain, not accompanied by general malaise and fever, nearly always mean syphilis of the interstitial variety.

In speaking of the vascular type of neurosyphilis, it was stated that hemiplegia is the most important representative of that type, while the meningitic group is represented by the cranial nerve syndrome.

In the older texts much has been said about gumma. What is a gumma? It is a collection of syphilitic deposits in a limited area and it produces its symptoms by mechanical pressure the same as a tumor mass. Gumma of the brain may appear very much like nonspecific tumor, with choked disk, gradually developing paralysis of either motion or sensation, or both. The treatment is the same as tumor from other causes. American and English surgeons are agreed that when a gumma has been definitely diagnosed and antispecific treatment has produced no results within a period of six weeks, the time for waiting has passed and only surgical intervention is left.

Cerebrospinal syphilis is another variety of interstitial neurosyphilis in which not only the brain but also the spinal cord is implicated. This is the most frequent type of neurosyphilis, for seldom is there seen a pure brain or cord syphilis; usually there is an admixture of symptoms belonging to both.

In the *cord* we may have *thrombosis,* with a pathology similar to that of the brain. There is the so-called myelomalacia—softening of the cord—corresponding to encephalomalacia—softening of the brain substance—both caused by thrombosis of diseased arteries. This cord disease is falsely called myelitis, a name which does not apply to the syphilitic type because it is not an inflammatory but a vascular disease. However, there is a cord disease produced by lues which is properly called meningomyelitis, in which, owing to pressure of inflammatory gummatous material found in meninges and cord substance, there are found distinct cord symptoms. As the posterior roots are almost always involved, sharp, excruciating pains appear early and are followed by anesthesia when the pressure has continued for a long time. So that we have a patient with pains in various portions of the body, which are worse at night; and when there are also changes in the reflexes, combined with positive serologic findings, we are confronted with syphilitic meningomyelitis.

Gumma of the cord is the rarest of luetic spinal cord diseases. It is practically a tumor of the spinal cord and gives symptoms similar to tumor of nonspecific origin. In addition we usually have some evidences of brain involvement, such as pupillary irregularities. The regional signs are the same as those of the nonspecific variety, but here again there may be differences, to detail which would require too much space.

Parenchymatous neurosyphilis: general paresis and tabes are the best known representatives of this variety. Before the true etiology was discovered, these were classed among the postsyphilitic or parasyphilitic disorders. We now know that they are as truly caused by spirochetes as is syphilitic inguinal adenitis.

Tabes is a degeneration of the posterior columns; whether it begins in the intervertebral ganglia or the posterior columns does not matter. It is a sensory neuron degeneration. There is never any loss of power in a case of locomotor ataxia or tabes, motor disturbances appearing rarely, and then only as a complication. The patient walks with a staggering gait, a double step; his walk is peculiar but not because he is powerless to walk well, for he has no motor weakness; the walk is due to sensory incoordination. For the same reason he will be unable to find his nose. Instead he points to the ear when asked to close his eyes and find his nose. There is never motor loss in tabes; it is always sensory. That is frequently forgotten. The beginning of the disease is insidious; very few can name its date, and it may take twenty-five, thirty, or forty years before it ends. The great hope of the tabetic is that he may live out his natural life before the end of the disease is reached. In the beginning there is destruction of few nerve fibers; this explains the little twinges of pain. The patient may suffer from lancinating pains in face, or leg. The disease begins by preference in the posterior columns of the lumbar and sacral cord, but it may begin higher up. From a diagnostic viewpoint the lancinating pains are extremely important, for when a patient comes to the office complaining of rheumatism, falsely called, and states that the rheumatism comes and goes, you are probably confronted with a case of tabes. Examine the pupils and the deep reflexes. I must emphasize in this place that the pupil examination is of far more importance in establishing the diagnosis of tabes or of syphilis in general than any other single symptom. Some people flash a light into the eyes, alarming the patient so that the pupils contract at once. This is the wrong technic. The pupillary light reflex is of such importance, that the correct method should be acquired by every one.

One could spend a great deal more time on the symptomatology of tabes, but I will say that when a patient comes to a physician's office complaining of genitourinary disturbances without apparent cause, of pains in the abdomen and of attacks of colic and vomiting, pains in the abdomen or in the region of the gall-bladder, in the appendix, or anywhere in the abdominal cavity, the case is not necessarily surgical. Dr. Nuzum, formerly of Cook County Hospital, has found that a number of cases of tabes with gastric crises were operated on for gall-stones, for appendicitis, and for intussusception of the bowel, when these conditions were really only simulated by crises. Some of our best surgeons have failed, not because of carelessness in technic, but because they did not examine the patient carefully before operation. I do not know of any neurologist who would be mistaken regarding a case of gastric crisis.

A point worthy of note is, that the tabetic does not always consult a neurologist; he goes to a specialist of some kind. Certainly the good ophthalmologist will discover tabes because he examines for light reflexes and inspects the eye-grounds. The genitourinary surgeon sins often, unless he is mindful of tabes. Some of these specialists will treat patients locally for bladder disturbances, when they ought to know that sphincter disturbances constitute an important symptom of tabes. The physician will treat his patient until he discovers that the treatment is not doing good, and then concludes it must be something else; finally the neurologist may be consulted. The greatest sinner of all is the general practitioner who treats the tabetic's "rheumatism." A patient comes to the office, "Doctor, I have terrible pains, will you give me something for rheumatism?" And without even looking at him the doctor prescribes salicylates, and it stops the pains, because they are over before he has left the office. He takes the prescription, has it refilled, and goes on for two or three years treating his rheumatism until somebody finds out that he has tabes instead of rheumatism.

General Paresis: A patient enters with the statement that 20 years ago he has had gonorrhea and chancre but no syphilis. He is fatigued, suffers pains in his back and all over; he cannot work as well as formerly. He knows there is something wrong with him. If the doctor is too busy to give him a thorough examination he says, "I know what the matter is, you are working too hard." "Yes, Doctor, I have not had a vacation in years. I am too active. If you tell me I need a vacation, I am going to take one." "You certainly do need a vacation." The doctor sends him off for two months in the country, thinking he is dealing with a neurasthenic. But that was not neurasthenia at all. It was the preparetic stage, that is the neurasthenic stage of general paresis, which often ushers in the true disease. The same patient may later come in and say, "I had a fit, and became unconscious." Similarly the physician may be called to see a patient who has had an "apoplectiform" attack and lost power in one half of the body. The doctor diagnoses "hemorrhage of the brain." The patient usually recovers rapidly, but this is the beginning of paresis. An examination reveals lapses of memory and other mental changes; where formerly the patient was liberal, he has become a miser; formerly a moral man, he has now become immoral. He brings a woman from the street into his house and in the most unabashed manner introduces her to his wife as his new sweetheart. Others of these patients boast of wonderful power; the most difficult things are possible for the paretic. Examine the pupils and you will discover an inequality; take the reflexes and you will find them exaggerated or unequal. This inequality of the reflexes and pupils is a sign of paresis. By all means have Wassermann tests made.

When a man who was always well balanced suddenly changes his conduct, moral principles, and shows poor judgment, paresis is probably the cause. Unfortunately the disease does not always appear with symptoms fully developed; there are those paretics whose actions are merely considered queer for a time. By the most stupid speculation, some have lost large amounts of money, the savings of a life-time, before they were discovered to be paretics.

Paresis, the most serious form of parenchymatous neurosyphilis, is not difficult to diagnose if both neurologic and mental tests are applied. Sometimes the mental examination alone will lead to a correct diagnosis and in other instances a neurologic examination enables the physician to detect early paresis in the face of few or no mental signs. Of course, one should never pronounce the ominous words "general paresis" in the absence of a positive Wassermann on either blood or spinal fluid. The clinical picture of general paresis may be simulated by alcoholism, lead encephalopathy, senility and by diffuse cerebral arteriosclerosis, the forms known as pseudoparesis.

TREATMENT

1. *Interstitial Neurosyphilis.* It is strange that the strongest advocates of the newer treatment by means of the various preparations of salvarsan should not have discarded mercury. The reason is evident; mercury is indispensable in the treatment of neurosyphilis. It now occupies the position formerly held by iodides. Mercury in some form occupies an important rôle in our therapeutic armamentarium against neurosyphilis, but it is especially valuable in interstitial neurosyphilis. The two methods now in vogue are, by inunction and injection. The old mercurial ointment still leads in the inunction treatment, though several newer preparations have become aspirants for recognition. If only to condemn it, I may mention the internal treatment of syphilis by means of little pills containing either green or red iodide of mercury. That treatment, happily a thing of the past with most of us, was an abomination; it fooled the patient and it fooled the doctor; the latter thought he was giving treatment and the former that he was taking treatment, when in reality he was only passing little pills through his intestines. The method of using inunction is so ancient that directions to physicians are superfluous, though I have noticed that physicians often fail to give proper directions to their patients.

The method of choice in the use of mercury is the injection of either soluble or insoluble mercury into the muscles. If the patient is in a position to take daily treatments, the soluble mercury is to be preferred. However, the rule is that patients are either unwilling or unable to see a physician daily. As a consequence, we are obliged to use insoluble mercury once or twice weekly. My personal preference is for the painless gray oil, first extensively used in England and recently made quite popular in this country by the National Pathological Laboratory. The preparation is sold in filled syringes, each containing sufficient for 10 injections. Injections may be given once or twice weekly, depending on the severity of the case. The usual landmark is, divide the line drawn from the upper end of the intergluteal depression to the anterior superior spine of the ilium, and inject at the point of division, introducing the needle perpendicularly down to a depth of two to three inches. The amount to be injected is about one to two grains weekly. While giving mercury, one should never omit ordering an acid-free diet, and the use of powdered chlorate of potash as a mouth-wash.

While brilliant results have been achieved from the intelligent use of mercury alone in the interstitial variety of neurosyphilis, the combination of mercury by intramuscular injection with some preparation of salvarsan intravenously administered, has given us uniformly the best results.

In the majority of cases of interstitial neurosyphilis the combined mercury-salvarsan treatment as outlined suffices. However, in those diffuse nervous lesions that have resisted the usual treatment, some form of intraspinal medication becomes necessary. This will be outlined under the next sub-heading.

2. *Parenchymatous Neurosyphilis.* In this group I take recourse to the autoserosalvarsan method of Swift Ellis, because the ordinary intravenous route gives unsatisfactory results. I shall not enter into a detailed description of this method, as this can now be found in any good textbook. However, I may mention that I have not found it necessary to make a hospital patient out of every case requiring the treatment. Patients can be treated in the office or laboratory on two successive days. After the intraspinal treatment the patient is instructed to take the quickest vehicle of transportation to reach home, then to lie on his back for twenty-four hours in a bed, the foot of which is elevated about six inches. This makes an immense saving of time and money to those who can and are obliged to work. For this reason I give the intravenous injection on Friday afternoon, the intraspinal one the next afternoon, and the patient rests in bed until Sunday noon and is ready to return to work Monday morning. The injection is repeated once weekly, and I have yet to see my first accident from the ambulatory method of giving the original or the Ogilvie-Swift-Ellis method of treatment.

A CLINICAL AND BIOCHEMICAL STUDY OF NEUROSYPHILIS

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PART II

The Arsenic Content of the Spinal Fluid after the Intravenous Administration of Silver Arsphenamine in Relation to the Type of Neurosyphilis

IN a previous communication[1] we presented a general review of the results of quantitative examinations for arsenic in 239 spinal fluids from 151 cases of neurosyphilis following the intravenous administration of silver arsphenamine. We demonstrated the presence of arsenic in the spinal fluid two hours after the intravenous administration of silver arsphenamine in 86 per cent of our cases in an average quantity of 11.548 mg. per cent. We also demonstrated its presence in 76 per cent of our cases at the end of seventy-two hours in an average quantity of 12.589 mg. per cent. The cases in which the amount of arsenic was sufficient for quantitative determination were slightly less, being 78 per cent and 68 per cent respectively. The difference represents cases in which the drug could be qualitatively demonstrated but not quantitatively measured and has been designated as a trace. This represents an amount less than one-half part per million.

Chart 1 shows graphically the curve of the average arsenic content at the several periods that were chosen for the examinations.

Table I illustrates the percentage of fluids and cases in which arsenic was qualitatively present. In this table the trace percentage is also shown. By subtraction one can calculate the proportion of fluids or cases in which a quantitative estimation was possible.

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[1] Am. Jour. Syph., Vol. vii, No. 2, April, 1923, pp. 287-317.

For the classification followed in grouping our cases we would refer the reader to our first publication on this subject.[1]

The results *en masse* indicate that arsenic passes into the spinal fluid within two hours after the intravenous administration of silver arsphenamine, that there is a reduction of the amount of arsenic in the spinal fluid between two and forty-eight hours and an in-

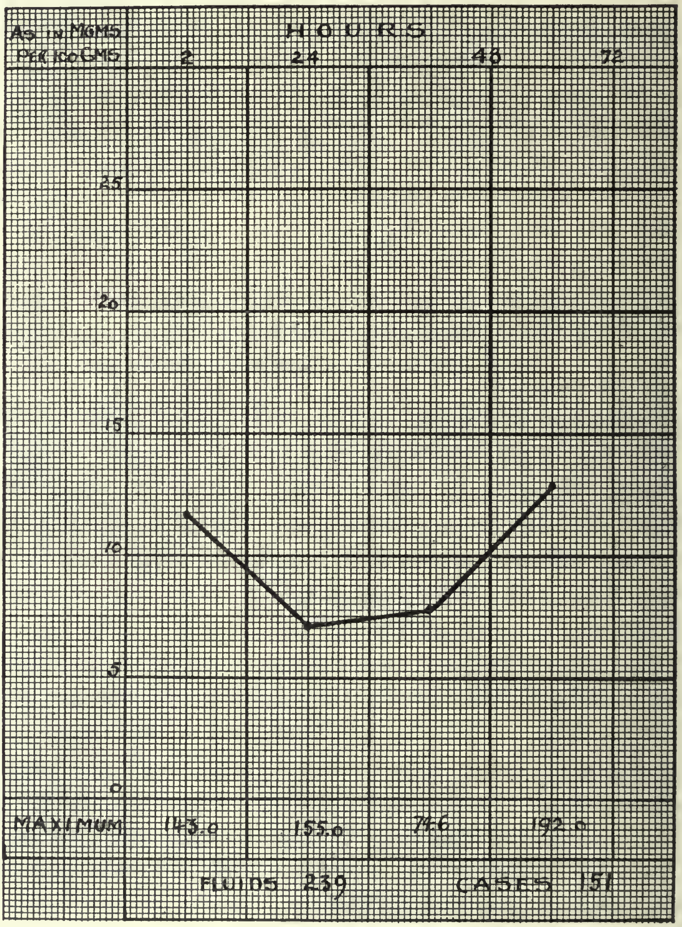

Chart 1.—Diversified group showing the curve of the average quantities of metallic arsenic in 239 spinal fluids from 151 cases of neurosyphilis in relation to the time interval between the intravenous administration of silver arsphenamine and lumbar puncture. Quantities are expressed in mg. per 100 gm. of dried specimen.

crease between forty-eight and seventy-two hours. Whereas this statement is correct if one considers only the totality of our results, it is only partially true when the results are analyzed separately for each type of neurosyphilis. It is the purpose of this paper to discuss that feature.

TABLE I

SHOWING THE PERCENTAGES, BY FLUIDS AND CASES, OF METALLIC ARSENIC IN A GROUP OF 239 FLUIDS FROM 151 DIVERSIFIED CASES OF NEUROSYPHILIS AT INTERVALS OF FROM 2 TO 72 HOURS AFTER THE INTRAVENOUS ADMINISTRATION OF SILVER ARSPHENAMINE.

HOURS	2		24		48		72	
	115 Fluids	62 Cases	45 Fluids	34 Cases	46 Fluids	30 Cases	33 Fluids	25 Cases
Present	89.%	85.5%	91.%	88.%	80.5%	70.%	82.%	76.%
Trace*	6.%	8.0%	13.%	18.%	6.5%	10.%	6.%	8.%

*Less than one-half part per million.

MESODERMAL GROUP

This group consisted of 104 fluids from 66 cases distributed as follows:

TABLE II

			AS. CONTENT IN MG. %	
INTERVAL	FLUIDS	CASES	MAXIMUM	AVERAGE
2 Hours	48	28	143.	14.4686
24 Hours	22	15	98.	10.554
48 Hours	19	11	26.4	7.4635
72 Hours	15	12	192.0	17.4834
	104	66		

The average arsenic content of the spinal fluid in this type of neurosyphilis was greater than the values shown in our mass analysis but the periodic results followed the same rule, i.e., a drop from two to forty-eight hours and a sharp rise at seventy-two hours. We have investigated the intervals that preceded the last arsphenamine administration for the purpose of determining the effect, if any, that this might have had. The case numbers refer to the tabulations accompanying our previous communication.[1]

TWO HOUR PERIOD

In the two hour group consisting of 48 fluids from 28 cases arsenic was present in 100 per cent of cases. The maximum amount of

143 mg. per cent came from a case of hypertrophic cervical meningitis. (No. 29 D. C.) No arsphenamine had been given to this patient for a period of twenty-five days previous to the administration for the purpose of this analysis, but during the four preceding months the treatment consisted of 6 silver arsphenamine, 2 arsphenamine and 15 mercurial injections. The clinical features indicated that the location of the pathology was in the meningeal coverings of the cord and the nerve roots, and we venture the presumption that the capillaries of the chorioid plexi and the spinal piarachnoid were not altered sufficiently to diminish their permeability to the drug. Treatment for 18 months rendered the fluid serology negative.

In no case did we fail to detect arsenic although in three fluids (Nos. 21, 47 and 48) from two cases it was present only in a trace.

Trace No. 21 A. B.—Cerebral meningovascular with beginning optic atrophy. Interval of 2 months since previous administration of arsphenamine.
Trace No. 47 P. P.—Cerebrospinal meningovascular. Interval of 6 weeks.
Trace No. 48 P. P.—Cerebrospinal meningovascular. Interval of 4 weeks.

The intervals of 4 to 8 weeks during which no arsphenamine had been administered in these cases might be thought of in explanation of the small amount found in the spinal fluid, were it not for the preceding case and others that will follow that contradict such an assumption. Case 21 was subject to intermittent psychotic episodes of a depressive nature that allied it closely to the group of manic depressive psychoses. The case represented by the Nos. 47 and 48 had deep seated lesions of the pyramidal tracts. After treatment for 30 and 18 months respectively the fluids became negative with the exception of the colloidal gold curves which remained elevated. The Wassermann reactions in the bloods changed from 4 plus to 1 plus and doubtful respectively.

TWENTY-FOUR HOUR PERIOD

In the twenty-four hour group consisting of 22 fluids from 15 cases arsenic was present in 87 per cent of the cases. The maximum amount of 98.0 mg. per cent was obtained in a case of cerebrospinal meningovascular syphilis (No. 8 C. B.). There had been an interval of 20 days since previous administration of arsphenamine. For four months preceding this rest period arsphenamine had been given at intervals of 7 to 14 days. On another occasion however (see No. 9 below) this same case, after a similar rest interval, showed only a trace of arsenic.

Arsenic was absent in 2 cases (Nos. 2 and 10) and present in trace in 3 cases (Nos. 9, 19 and 21).

Absent No. 2 H. A.—Cerebrospinal meningovascular. Interval of 7 months.
Absent No. 10 M. G.—Cerebrospinal meningovascular. Interval of 12 days.
Trace No. 9 C. B.—Cerebrospinal meningovascular. Interval of 19 days.
Trace No. 19 H. R.—Cerebral meningovascular. Interval of 22 days.
Trace No. 21 J. S.—Cerebrospinal meningovascular. Interval of 29 days.

The first of the above five cases was a male, aged forty, with clinical evidence of cerebral endarteritis. Twelve months of treatment had rendered all serology except the spinal fluid Wassermann negative. Clinical improvement was manifest for a few months, but death ensued eventually from cerebral hemorrhage. In the third case, 28 months of persistent treatment failed to alter the Wassermann reaction in the blood or spinal fluid. The fourth case was always serologically negative but suffered from the anxiety type of psychoneurosis. The fifth case was one with deep seated pyramidal tract lesions. The Wassermann reaction in the blood and spinal fluid remained positive after 15 months of treatment.

FORTY-EIGHT HOUR GROUP

The forty-eight hour group consisted of 19 fluids from 11 cases. Arsenic was present in 91 per cent of the cases.

The maximum quantity of 26.4 mg. per cent was obtained in a case of hypertrophic cervical meningitis (No. 8 D. C.). Previous to this administration no arsphenamine had been given for three weeks. This is the same case that had the highest arsenic content in the two hour group the interval being approximately the same. Arsenic was absent in two fluids (Nos. 17 and 19) from one case, and present in trace in two cases (Nos. 2 and 49).

Absent No. 17 J. S.—Cerebrospinal meningovascular. Interval of 17 days.
Absent No. 19 J. S.—Cerebrospinal meningovascular. Interval of 22 days.
Trace No. 2 G. H.—Cerebral meningeal. Interval of 11 days.
Trace No. 49 S. W.—Cerebral meningovascular. Interval of 1 year.

The fluid of J. S. represented by Nos. 17 and 19, after intensive treatment for 11 months, became serologically negative except for the colloidal gold. The second case G. H. was one of probable gummatous meningitis with epileptiform seizures. After 18 months of therapy the spinal fluid became negative but the blood Wassermann remained three plus. The third case S. W. showed but little alteration in the spinal fluid serology after nine months of persistent therapy. With the exception of this case the interval could not account for the quantitative results.

SEVENTY-TWO HOUR GROUP

In the seventy-two hour group consisting of 15 fluids from 12 cases arsenic was present in 75 per cent of cases.

The maximum quantity of 192 mg. per cent represented the largest amount discovered in any case of our whole series. This result was obtained in a case of cerebral meningeal syphilis (No. 2 E. R.). For 24 days preceding the injection no arsphenamine had been administered. Further details of this case have been given in a previous communication.[1]

Arsenic was absent in three cases (Nos. 4, 8 and 15), and present in trace in two cases (Nos. 7 and 13).

Absent No. 4 A. B.—Cerebral meningovascular with beginning optic atrophy. Interval of 10 days.
Absent No. 8 D. F.—Cerebral meningovascular with bilateral optic atrophy. Interval of 26 days.
Absent No. 15 J. S.—Cerebrospinal meningovascular. Interval of 11 days.

Trace No. 7 P. P.—Cerebral meningovascular. Interval of 11 days.
Trace No. 13 C. B.—Cerebrospinal meningovascular. Interval of 10 days.

Again it does not seem justified to attribute the low arsenic content in these cases to the intervals between arsphenamine administration. The first case, A. B., showed only a trace in an examination at the two hour period. The second case, D. F., was one of bilateral optic atrophy. The third case, J. S., had no arsenic in two examinations at the 48 hour period. The fourth case, P. P., showed only a trace of arsenic on two occasions at the two hour period. The fifth case, C. B., had previously shown a considerable variability.

In order to ascertain if there were any noticeable variations in relation to the topographical location of the pathology we subgrouped our cases as shown in Table III. In our opinion the differences noted in this respect could be attributed entirely to the numerical variation.

TABLE III

SHOWING THE AVERAGE QUANTITIES OF METALLIC ARSENIC IN 104 FLUIDS FROM 66 CASES OF MESODERMAL NEUROSYPHILIS IN RELATION TO THE TOPOGRAPHICAL LOCATION OF THE PATHOLOGY. QUANTITIES ARE EXPRESSED IN MG. PER 100 GM. OF DRIED SPECIMEN.

INTERVALS	CEREBRAL			SPINAL			CEREBROSPINAL		
	FLDS.	CASES	AVERAGE	FLDS.	CASES	AVERAGE	FLDS.	CASES	AVERAGE
2 Hours	27	18	11.497	5	3	30.312	16	7	14.4075
24 Hours	4	4	6.4225	1	1	3.2	17	10	11.9588
48 Hours	5	3	6.3474	1	1	1.0	13	7	8.389
72 Hours	9	7	26.563	2	1	11.15	4	4	0.221
	45	32		9	6		50	28	

TABLE IV

SHOWING THE PERCENTAGES, BY FLUIDS AND CASES, OF METALLIC ARSENIC IN 104 FLUIDS FROM 66 CASES OF MESODERMAL NEUROSYPHILIS AT INTERVALS OF FROM 2 TO 72 HOURS AFTER THE INTRAVENOUS ADMINISTRATION OF SILVER ARSPHENAMINE.

HOURS	2		24		48		72	
No	48 Fluids	28 Cases	22 Fluids	15 Cases	19 Fluids	11 Cases	15 Fluids	12 Cases
Present	100.%	100.%	91.%	87.%	95.%	91.%	80.%	75.%
Trace*	6.%	7.%	13.5%	20.%	10.5%	18.%	13.%	17.%

*Less than one-half part per million.

Chart 2 shows the curve of the average arsenic content at the several periods and Table IV the percentages by fluids and cases.

In the type of neurosyphilis in which the lesions are confined for the most part to the mesodermal tissues arsenic, from a silver arsphenamine base, penetrates the spinal fluid promptly after intravenous administration. In early cases where the pathology is

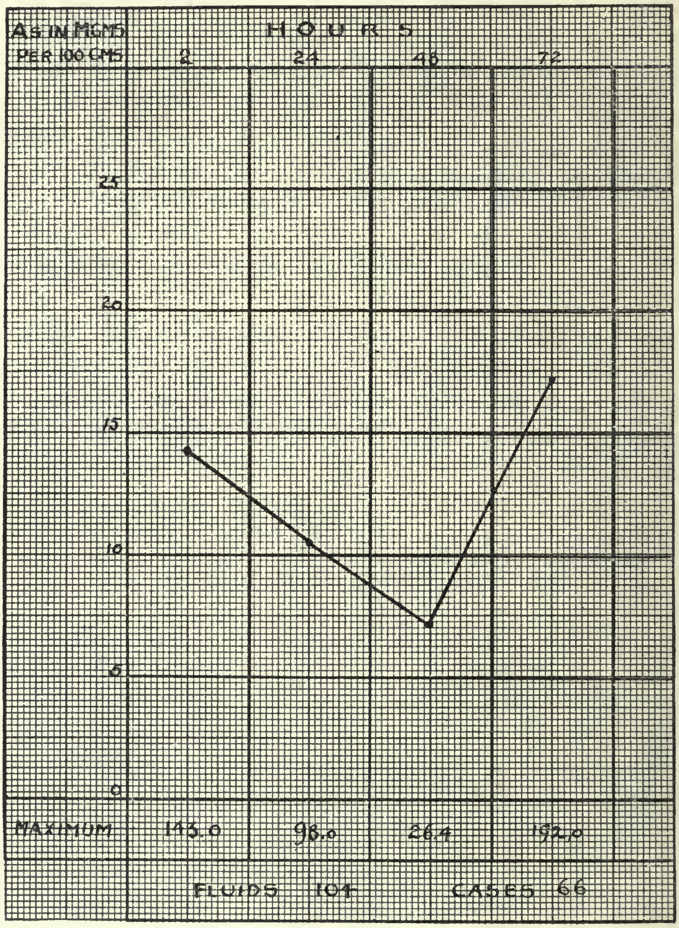

Chart 2.—Mesodermal group showing the curve of the average quantities of metallic arsenic in 104 fluids from 66 cases of mesodermal neurosyphilis in relation to the time interval between the intravenous administration of silver arsphenamine and lumbar puncture. Quantities are expressed in mg. per 100 gm. of dried specimen.

confined to the superficial structures the quantity of arsenic in the spinal fluid is greater, but as the invasion becomes more extensive, the penetrability becomes lessened. Some cases of long standing infection show consistently low penetrability while others show extreme variability. The cases cited below will illustrate this.

Case 1.—E. R. Cerebral meningeal syphilis. Acute syphilitic meningitis of the convexity of the cerebral hemispheres originating about one year after infection and after eleven months of intensive therapy. The pathology was confined to the superficial coverings of the nervous system and the permeability for arsenic was good.

2 hours	17.7 mg. per cent
2 hours	18.3 mg. per cent
2 hours	20.4 mg. per cent
72 hours	4.8 mg. per cent
72 hours	192.0 mg. per cent
72 hours	4.2 mg. per cent
Average	42.85 mg. per cent

Case 2.—D. C. Spinal meningeal syphilis. Hypertrophic cervical meningitis with amyotrophism of both upper extremities. The pathologic lesions were confined to the meninges and nerve roots. The permeability for arsenic was good.

2 hours	143. mg. per cent
24 hours	3.2 mg. per cent
48 hours	1.0 mg. per cent
72 hours	19.3 mg. per cent
72 hours	3.0 mg. per cent
Average	33.9 mg. per cent

Case 3.—C. B. Cerebrospinal meningovascular syphilis, of diffuse distribution. There was a fair average permeability but marked variations occurred.

2 hours	16. mg. per cent
2 hours	12.9 mg. per cent
24 hours	2.9 mg. per cent
24 hours	98.0 mg. per cent
24 hours	Trace
48 hours	2.08 mg. per cent
48 hours	4.99 mg. per cent
48 hours	10.5 mg. per cent
72 hours	Trace
Average	16.66 mg. per cent

Case 4.—G. H. Cerebral meningovascular syphilis, chronic syphilitic meningitis of the convexity of the cerebral hemispheres with probable extension into the

cortical substance causing epileptiform seizures. The deeper invasion in this case is apparently reflected in the lessened permeability for arsenic.

2 hours	4.3 mg. per cent
2 hours	0.8 mg. per cent
2 hours	5.7 mg. per cent
48 hours	Trace
48 hours	1.0 mg. per cent
Average	2.36 mg. per cent

ECTODERMAL GROUP

This group comprised 108 fluids from 67 cases distributed as follows:

TABLE V

	ECTODERMAL			
			AS. CONTENT IN MG.%	
INTERVAL	FLUIDS	CASES	MAXIMUM	AVERAGE
2 hours	52	26	113.0	9.0219
24 hours	19	15	66.3	8.6076
48 hours	22	15	74.6	8.654
72 hours	15	11	11.4	4.4236
	108	67		

TWO HOUR PERIOD

Arsenic was present in 73 per cent of the 26 cases. The fluid examinations numbered 52. The maximum amount of arsenic was 113. mg. per cent. This case, No. 94 L. P., was one of tabes dorsalis and this result was obtained after a rest interval of 41 days. Previous to this interval arsphenamine had been administered practically without interruption for 11 months. With the exception of occasional rest periods this patient has been under treatment for 4½ years. At the time that he first came under our observation he had experienced psychotic episodes suggestive of general paresis. Despite a large amount of treatment over a long period, Wassermann reactions in blood and spinal fluid have remained positive, and the colloidal gold reactions have been of the so-called paretic type.

Arsenic was absent in nine fluids from seven cases and present only in trace in 3 fluids from 2 cases:

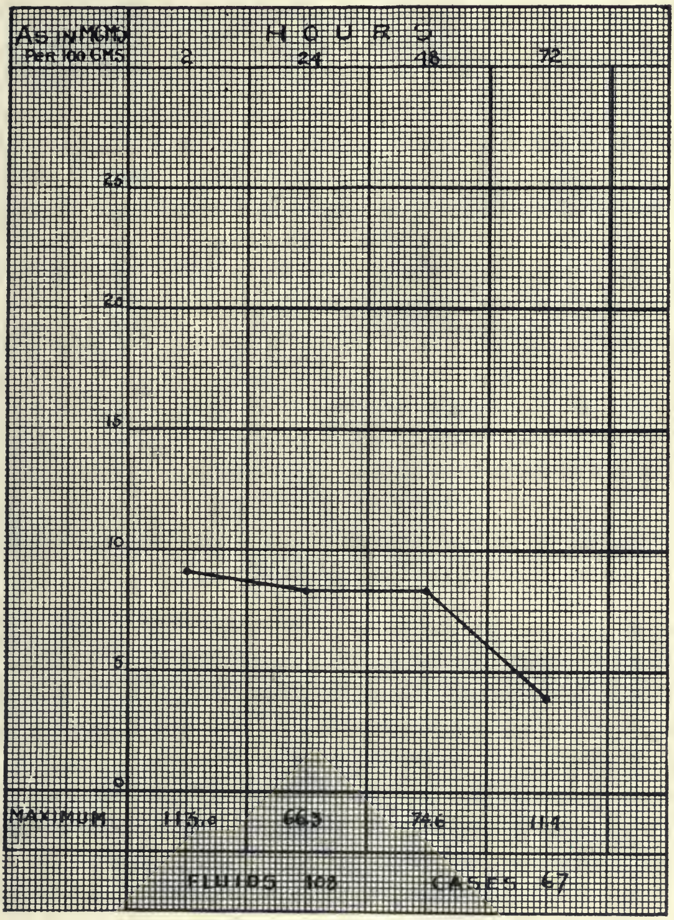

Chart 3.—Ectodermal group showing the curve of the average quantities of metallic arsenic in 108 fluids from 67 cases of ectodermal neurosyphilis in relation to the time interval between the intravenous administration of silver arsphenamine and lumbar puncture. Quantities are expressed in mg. per 100 gm. of dried specimen.

Absent No. 61 J. M.—Cerebral parenchymatous. Paretic syndrome. Interval of 14 days.

Absent No. 62 F. B.—Cerebral parenchymatous. Paretic syndrome. Interval of 5 days.

Absent No. 63 F. B.—Cerebral parenchymatous. Paretic syndrome. Interval of 7 days.

Absent No. 77 J. G.—Spinal parenchymatous. Tabetic syndrome.
Interval of 16 days.
Absent No. 78 J. G.—Spinal parenchymatous. Tabetic syndrome.
Interval of 12 days.
Absent No. 83 LeB.—Spinal parenchymatous. Tabetic syndrome.
Interval 12 days.
Absent No. 87 H. M.—Spinal parenchymatous. Tabetic syndrome.
Interval of 19 days.
Absent No. 98 J. R.—Spinal parenchymatous. Tabetic syndrome.
Interval of 7 days.
Absent No. 100 J. T.—Spinal parenchymatous. Tabetic syndrome.
Interval of 46 days.
Trace No. 67 C. C.—Spinal parenchymatous. Tabetic syndrome.
Interval of 10 days.
Trace No. 68 C. C.—Spinal parenchymatous. Tabetic syndrome.
Interval of 15 days.
Trace No. 75 J. G.—Spinal parenchymatous. Tabetic syndrome.
Interval of 13 days.

The two cases of paresis have died. Of the six cases of tabes dorsalis four appear to be completely arrested clinically and the other two have been relieved of all acute symptoms. The serology has become completely negative in two cases, is improved in three, and is unchanged in one case. This entire group represents deep seated degenerative pathology of long standing. Chronic vascular changes may account for this failure of the arsenic penetration.

TWENTY-FOUR HOUR PERIOD

This group consisted of 19 fluids from 15 cases. In 87 per cent of the cases arsenic was present. The maximum amount was 66.3 mg. per cent Case 41—G. W. Spinal parenchymatous-tabetic syndrome. No arsenic had been administered for six months. The tabetic symptoms had been subjectively present for only a few weeks. The previous treatment had consisted of twelve arsphenamine and 19 mercurial injections during a period of 18 months. The blood Wassermann had been changed from 4 plus to 1 plus, but the spinal fluid was positive: cells 25, globulin two plus, Wassermann three plus in 1.0 c.c., colloidal gold 2333210000.

The good permeability indicated by the first result in this case augured well for therapeutic expectancy and the result has justified the optimism with which intensive intravenous and intraspinous therapy was instituted. The cell count, globulin and colloidal gold reactions became negative after three months' treatment consisting of 7 silver arsphenamine, 2 neoarsphenamine and 4 Swift-Ellis treatments. The spinal fluid Wassermann is still positive after nine months of treatment, but there has been complete relief of all subjective symptoms.

Arsenic was absent in two cases and present in trace in 2 cases:

Absent No. 27.—A. S. Cerberal parenchymatous. Interval of 23 days.
Absent No. 30.—C. C. Spinal parenchymatous. Tabetic syndrome. Interval of 27 days.
Trace No. 28.—P. B. Spinal parenchymatous. Tabetic syndrome. Interval of 9 days.
Trace No. 40.—B. L. Spinal parenchymatous. Tabetic syndrome. Interval of 90 days.

The rest from arsenic for comparatively long periods might have something to do with these results, but again this assumption is contradicted by the result in No. 41 G. W. that has been discussed above, and further by the fact that patient A. S. in whose fluid no arsenic could be detected at the twenty-four hour period, showed 74.6 mg. per cent at the forty-eight hour period after a rest interval of 48 days. One of the above cases of tabes dorsalis, C. C., has been arrested and rendered serologically negative. The other two have been improved clinically and serologically.

FORTY-EIGHT HOUR PERIOD

This group consisted of 22 fluids from 15 cases. In 60 per cent of the cases arsenic was present. The maximum amount was 74.6 mg. per cent. Case 28 A. S. Cerebral parenchymatous. This result occurred after a rest from arsphenamine of 48 days. The same case had no arsenic on one examination at the twenty-four hour period after a rest of 23 days, and none on one occasion at the forty-eight hour period after a 28 day rest. Thus it is apparent that in this case there was considerable variation in the permeability for arsenic.

Arsenic was absent in 6 cases and present in trace in 2 cases:

Absent No. 27.—T. P. Cerebral parenchymatous. Paretic syndrome. Interval of 48 days.

Absent No. 29.—A. S. Cerebral parenchymatous. Interval of 28 days.

Absent No. 31.—N. A. Spinal parenchymatous. Tabetic syndrome. Interval of 17 months.

Absent No. 32.—E. G. Spinal parenchymatous. Tabetic syndrome. Interval of 50 days.

Absent No. 36.—L. P. Spinal parenchymatous. Tabetic syndrome. Interval of 9 days.

Absent No. 46.—J. T. Spinal parenchymatous. Tabetic syndrome. Interval of 5 days.

Trace No. 35.—L. O. Spinal parenchymatous. Tabetic syndrome. Interval of 7 days.

Trace No. 37.—L. P. Spinal parenchymatous. Tabetic syndrome. Interval of 7 days.

The case of paresis has died. The second case of cerebral parenchymatous syphilis has been discussed above. Of the five cases of tabes attention should be called to Nos. 36 and 37. These fluids came from the same case (L. P.) that showed 113 mg. per cent at the two hour period and is discussed there. In our opinion this case clinically and serologically is a potential paretic and the persistent treatment, we believe, has prevented the clinical development of this syndrome. The clinical results in the other four cases have been satisfactory.

SEVENTY-TWO HOUR PERIOD

Fifteen fluids from 11 cases were examined. Arsenic was present in 82 per cent of the cases. The maximum quantity of 11.4 mg. per cent came from a case of tabes dorsalis, No. 30 G. The rest interval was 7 days.

Two cases were negative for arsenic.

No. 20 M.F. Spinal parenchymatous. Tabetic syndrome. Interval of 35 days.

No. 33 L. O. Spinal parenchymatous. Tabetic syndrome. Interval of 7 days.

Table VI shows an analysis of this group in accordance with the topographical location of the pathology. The number in the spinal group is sufficiently large to warrant consideration and it will be noted that the average arsenic content diminished from the two hour to the seventy-two hour period.

Table VI

Showing the average Quantities of Arsenic in 108 Fluids From 67 Cases of Ectodermal Neurosyphilis in Relation to the Topographical Location of the Pathology. Quantities are Expressed in mg. Per 100 gm. of Dried Specimen.

	CEREBRAL			SPINAL			CEREBROSPINAL		
INTERVAL	FLDS.	CASES	AVERAGE	FLDS.	CASES	AVERAGE	FLDS.	CASES	AVERAGE
2 hours	4	3	0.8975	42	20	10.745	6	3	14.26
24 hours	2	2	0.86	15	11	9.0016	2	2	8.9
48 hours	4	3	19.5425	16	10	5.8137	2	2	9.65
72 hours	1	1	1.65	14	10	3.5608	0	0	0.
	—	—		—	—		—	—	
	11	9		87	51		10	7	

In our cases of ectodermal neurosyphilis, a few of which are given below, there was a lower index of permeability for arsenic than in the cases representing a more superficial localization of the pathologic changes.

Case 1.—F. B. Cerebral parenchymatous syphilis, paretic syndrome.

24 hours	0 mg. per cent
24 hours	0 mg. per cent
Average	0 mg. per cent

Case 2.—J. G. Tabes dorsalis.

2 hours	Trace
2 hours	0.8 mg. per cent
2 hours	0.0 mg. per cent
2 hours	0.0 mg. per cent
24 hours	19.5 mg. per cent
72 hours	1.13 mg. per cent
72 hours	9.13 mg. per cent
72 hours	1.84 mg. per cent
Average	4.05 mg. per cent

Case 3.—C. C. Tabes dorsalis.

2 hours	6.2 mg. per cent
2 hours	Trace
2 hours	Trace
Average	2.06 mg. per cent

Case 4.—M. F. Tabes dorsalis.

2 hours	0.7 mg. per cent
48 hours	4.4 mg. per cent
48 hours	4.5 mg. per cent
48 hours	3.5 mg. per cent
72 hours	0.0 mg. per cent
Average	2.6 mg. per cent

Case 5.—LeB. Tabes dorsalis.

2 hours	2.05 mg. per cent
2 hours	0.0 mg. per cent
72 hours	1.05 mg. per cent
Average	1.03 mg. per cent

Case 6.—M. Tabes dorsalis.

2 hours	4.2 mg. per cent
2 hours	0.0 mg. per cent
2 hours	5.1 mg. per cent
Average	3.1 mg. per cent

Case 7.—J. T. Tabes dorsalis.

2 hours	0.0 mg. per cent
24 hours	14.4 mg. per cent
48 hours	16.03 mg. per cent
48 hours	0.0 mg. per cent
72 hours	0.804 mg. per cent
Average	6.205 mg. per cent

This group, then, including for the most part syndromes of paresis, tabes dorsalis and taboparesis differed strikingly from the mesodermal group. The amount of arsenic in the spinal fluid was definitely smaller, being less at the end of the two hour period by over 5 mg. per cent, about equal at 24 and 48 hours, and at the 72 hour period the difference was 13 mg. per cent.

The two groups were nearly identical in size and the striking difference in the quantitative results challenges us to give some explanation. Our first inference is that there is a diminution in the permeability of the capillaries of the chorioid plexus and piarachnoid. The arsenic enters the spinal fluid less easily, therefore less rapidly. Before very much passes from the blood to the spinal fluid it probably enters into more or less stable combination with the other tissues—skin, liver and kidneys. At the time when it is released by these tissues and again enters the blood stream, the relative impermeability of the chorioid plexus and pia arachnoidal capillaries permits it to be excreted before it can pass from the blood to the spinal fluid.

One is led to query if the neural tissues retain some of the arsenic in more or less stable combination and later discharge it into the spinal fluid. By analogy one might reason that when arsenic will not pass into the spinal fluid it will not pass into the neural tissues. This view, we believe, requires confirmation before it can be accepted and we are investigating this point.

Chart 3 and Table VII summarize the findings in the ectodermal cases.

TABLE VII.—ECTODERMAL

SHOWING THE PERCENTAGES, BY FLUIDS AND CASES, OF METALLIC ARSENIC IN 108 FLUIDS FROM 67 CASES OF ECTODERMAL NEUROSYPHILIS AT INTERVALS OF FROM 2 TO 72 HOURS AFTER THE INTRAVENOUS ADMINISTRATION OF SILVER ARSPHENAMINE.

HOURS	2		24		48		72	
	52 Fluids	26 Cases	19 Fluids	15 Cases	22 Fluids	15 Cases	15 Fluids	11 Cases
Present	83.%	73.%	90.%	87.%	60.%	60.%	87.%	82.%
Trace*	6.%	8.%	10.%	13.%	20.%	20.%	0.%	0.%

*Less than one-half part per million.

MIXED GROUP

This group consisted of 22 fluids from 13 cases distributed as follows:

TABLE VIII.—MIXED GROUP

			AS. CONTENT IN MG. %	
INTERVAL	FLUIDS	CASES	MAXIMUM	AVERAGE
2 hours	11	4	46.6	10.7781
24 hours	3	3	155.0	1.76
48 hours	5	4	11.5	6.354
72 hours	3	2	73.0	26.413
	22	13		

The number of examinations at this period was small, comprising only 11 fluids from 4 cases, in 50 per cent of which arsenic was present. The maximum quantity was 46.6 mg. per cent. (No. 57 M. W.) came from a case with bilateral optic atrophy. There had been an interval of 28 days since the preceding administration of arsphenamine.

Arsenic was absent in four fluids from two cases and present in trace once.

Absent 55—M. W. Same case as above—Interval of 1 month.

Absent 56—M. W. Same case as above—Interval of 28 days.
Absent 50—W. E. Same diagnosis as above case—Interval of 5½ months.
Absent 51—W. E. Same diagnosis as above case—Interval of 2¼ months.
Trace 54—M. W. Same case as above—Interval of 14 days.

It will be noted that both of these cases suffered with bilateral optic atrophy, and whereas on one examination the fluid of M. W. contained 46.6 mg. per cent of arsenic, on two occasions arsenic was absent and once it was present only in trace. These facts suggest the inference that the type and distribution of the pathology might account for the results.

TWENTY-FOUR HOUR PERIOD

Only three fluids were examined at this period arsenic being present in all of them. The maximum of 155.5 mg. per cent represents the second largest quantity found in any of our examinations to date. This case (No. 24 T. S.) was one of bilateral optic atrophy. The rest interval preceding the last arsphenamine administration was 5 months.

One fluid yielded only a trace (No. 23 M. W.), the rest interval having been 10 days. This was the same case that yielded 46.6 mg. per cent once, two negatives, and one trace, at the two hour period.

FORTY-EIGHT HOUR PERIOD

The number was again small consisting of 5 fluids from 4 cases. The maximum quantity was only 11.5 mg. per cent. It was from a case of bilateral optic atrophy (No. 24 Z). The rest interval had been a year.

Arsenic was absent twice:

No. 6.—Del V. Cerebral endarteritis—Interval 24 days.
No. 25.—A. N. Cerebrospinal—Amyotrophy. Interval 4 months.

SEVENTY-TWO HOUR PERIOD

This number was also small. Only 3 fluids from 2 cases were examined. Arsenic was present in all. The maximum of 73 mg.

per cent was obtained from the case of bilateral optic atrophy (No. 17 Z) that showed 11.5 mg. per cent at the forty-eight hour period. The rest interval had been two months.

The clinical diagnoses of the mixed group were as follows:

	Cases	Fluids
Optic Atrophy	9	17
Paretic syndrome	2	2
Cerebral endarteritis	1	2
Amyotrophy	1	1
	13	22

While the group is too small to warrant definite conclusions, certain points deserve mention.

Over two-thirds of the cases were optic atrophy and approximately 60 per cent of these yielded only a trace of arsenic or none at all. This is significant in the light of the clinical progressiveness of this condition.

CONCLUSIONS

1. There is a significant difference in the chemical physiology of arsenic in the various types of neurosyphilis.

2. When the lesions are essentially confined to the mesodermal structures arsenic can be detected in 80 to 100 per cent of fluids; as compared with 60 to 90 per cent when the ectodermal tissues are involved.

3. In mesodermal syphilis quantitative determinations can be made in 67 to 94 per cent of fluids, as compared with 40 to 87 per cent in ectodermal syphilis.

4. The average quantity of arsenic in the spinal fluid in mesodermal syphilis is 14 to 17 mg. per cent; in ectodermal 4 to 9 mg. per cent.

5. In mesodermal syphilis the quantity of arsenic in the spinal fluid is greatest at intervals of two and seventy-two hours after intravenous administration of silver arsphenamine, the average amount after seventy-two hours being slightly in excess of that found after two hours.

6. In ectodermal neurosyphilis the largest amount is present two hours after intravenous administration, diminishing at subsequent periods.

GASTRIC AND INTESTINAL SYPHILIS. REPORT OF A CASE. CLINICAL COURSE AND MORBID PATHOLOGY

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GASTRIC SYPHILIS

IN 1912 Meyers,[23] reviewing the literature of gastric syphilis, collected and analyzed sixty cases. Since then relatively large series have been reported by Einhorn,[8] Downes,[7] LeWald,[20] Smithies[35] and Eustermann[9] and many smaller groups by others. The largest series reported and probably the most critical analysis is the second paper by Eustermann which included the twenty-three of his original article with seventeen additional instances of the disease. In 1915 Smithies found seventy cases which he considered authentic, of which twenty-five were from the United States in the six years prior to that date. A review of the literature by Eustermann in 1918 showed the number of cases clinically diagnosed as syphilis of the stomach to be approximately two hundred. This author points out the discrepancy between the relative rarity of the condition as seen by the pathologist, and the apparent more common incidence as reported by the clinician, and proposes that this is more apparent than real considering the great frequency of the syphilitic infection. Eustermann states, "In a review of the literature I found that only a dozen or more of the cases clinically diagnosed syphilis of the stomach have been verified by histologic examination," and adds that Symmers,[36] who found only one syphilitic ulcer of the stomach in four thousand eight hundred and eighty necropsies, including three hundred fourteen syphilitics, was not inclined to accept the diagnosis unless confirmed by histology. Since the report of Eustermann about fifty additional clinical instances have been reported, and most of them may be considered authentic.

We are often reminded by the pathologist that clinical medicine is not an exact science. However, with a well-marked clinical picture such as has been described by the various authors above mentioned, and fulfilment of the requirements laid down by Chase,[5] often as certain a clinical diagnosis can be made as is possible in many conditions which have been recognized much longer and which are much more common and therefore better known, such as simple ulcer and carcinoma. The diagnosis may require a more careful and comprehensive study.

We would insist upon the following as of the greatest importance: (1) proof of the existence of syphilis, not only by the Wassermann test but by the finding of other evidences of syphilis within the body, or a reasonably certain clinical history of primary and secondary or tertiary lesions (if the Wassermann test be negative); (2) the demonstration of a gastric lesion by the usual clinical methods including the x-ray; (3) not only symptomatic but objective therapeutic improvement; (4) the clinical course of the disease.

As shown by Fowler[13] in his recent review and resumé of the literature concerning the diagnosis of organic gastric syphilis, a positive Wassermann with a definite gastric lesion does not prove that the lesion in the stomach is essentially syphilitic, and that indubitable instances of syphilitic disease of the stomach have been discovered in the absence of a positive blood serum test.

The characteristics of the roentgen shadow have been well described by Carman[4] who, no doubt, has had the opportunity of examining personally the largest number. He admits that though there are certain rather typical deformities which are relatively infrequent in other forms of gastric disease, and which seem to depend upon the peculiar pathology of syphilis in producing fibrous changes with contracture and stenosis and stiffening of the walls, with lessened pliability and absence of peristalsis, there is no pathognomonic roentgenologic sign.

It is a well recognized fact that symptomatic improvement, especially subjective, occurs as a rule in the various visceral manifestations of syphilis following efficient active therapy. Patients with syphilis of the liver, spleen, bone, central nervous system and cardiovascular system regain appetite and weight, improve in color, and in general appearance, and in their subjective feelings. Such therapeutic results we should expect to find in all individuals with gastric syphilis who receive sufficient vigorous antiluetic treatment in the form of intravenous therapy with diarsenol, combined with mercury administered in its various forms, and potassium iodid by mouth. We should also hope for an improvement in the gastric pathology as interpreted from the roentgen shadow. However, if the essential pathology of the gastric lesion is considered, it is not difficult to see that as a part of the healing process deformities and mechanical difficulties may actually develop or increase, for as the gummatous process heals a contracting and, therefore, frequently stenosing scar is formed. This effect cannot be differentiated from that of a progressive lesion of the proliferative type, such as carcinoma.

The course of the disease differs from cancer of the stomach in that there is not the steady and continuous progress to a fatal termination. Cachexia is less common and less marked in syphilis of the stomach than in cancer of the stomach.

The pathology has been described in some detail by Downes and LeWald, Eustermann, Morgan,[24] Symmers and McNeil in this country, and their reports reviewed by Fowler. The gross pathology is frequently such that at exploration the surgeon cannot distinguish between malignancy and syphilis of the stomach. Unless the local glands contain carcinomatous tissue an excised gland from the neighborhood of the lesion may not serve to make a correct diagnosis. The changes in the glands may be simple inflammatory in either condition, if there is an ulceration of the gastric mucosa. In a patient recently examined there were external and systemic evidences of syphilis, positive Wassermann tests, and an extensive gastric pathology. For a time the patient improved with antisyphilitic treatment. A postmortem examination revealed tertiary lesions with scarring of the liver and an extensive gastric carcinoma.

The clinical picture has been analyzed in the reports of the larger series. There is one detail of the routine examination of gastric conditions which is not discussed by any of the authors excepting Brown and Gaither,[3] namely, the testing of the stools for occult blood. ''Hematemesis is rarely present while melena in the majority of cases is absent, although if the tumor mass ulcerates, blood (usually occult blood at least) is noted.'' We have reason to believe that the presence or absence of occult blood in the stools and gastric content is of considerable value in differentiating syphilis from cancer, provided the stools are examined over a considerable period. The cancer is likely to ooze sufficient blood to give positive tests for blood, and more or less continuously, though not invariably. The gummatous ulcer may bleed, but rarely continuously, and especially not after specific treatment is well instituted.

INTESTINAL SYPHILIS

Very few instances of syphilis of the small bowel have been reported clinically, though syphilitic lesions of the colon, and more especially the lower sigmoid and rectum, are more common. The literature concerning syphilitic lesions of the small bowel is very meager. No clinical series of any size has been reported, but rather single instances. The early literature is well reviewed by Neumann[26] in the Volume on Syphilis in the Nothnagel System, and the gross pathology of the ulcerative type described from the case reports of E. Muller (1858) and Oser (1871). Fraenkel, in an analysis of 19,000 postmortem examinations covering a period of ten years, found only three cases, all of which had been wrongly diagnosed clinically. Oberndorfer in 1900 was able to collect only twenty-four authentic cases of intestinal syphilis, of which sixteen were of the small bowel alone and two of the small and large bowel.

The symptomatology of intestinal syphilis has been described by Neumann and more recently by Simon,[33] Brown and Gaither, and Wile.[38] The descriptions of the symptoms as given by Simon and by Wile are from a review of the cases described in the literature, chiefly continental. In 1917 Mortimer[25] reported a case of syphilis of the duodenum, and discusses syphilis of the small intestine. Syphilis of the duodenum should be considered along with gastric syphilis, in as much as the symptomatology and pathology are more nearly related to those of gastric syphilis. In the more recent literature we find a report of two instances of ulcerative intestinal lesions diagnosed as syphilis of the intestine by Haller and Walker,[18] and one by Scott and Pearson.[32] These three cases are not proven but the results of specific therapy were the strongest indication of their syphilitic nature. In the example reported by Scott and Pearson the Wassermann test was negative, but there was a definite syphilitic history and the condition responded to antiluetic treatment.

Two forms of the disease are recognized: (1) an early acute catarrhal enteritis, occurring as a part of the secondary exanthema, a general visceral roseola, with the symptoms of any acute catarrhal enteritis; (2) late involvement or tertiary lesions with symptoms usually like those of other forms of ulcerative enterocolitis. In addition to the symptoms depending upon the ulceration, there may arise additional symptoms depending upon the formation of an abdominal tumor (large gumma formation), and during the ulcerative process, and following it, the obstructive signs and symptoms resulting from healing of ulcers with stenosis. The usual symptom is a severe diarrhea with colicky pains, tenesmus, with mucus, pus and blood in the stools. There may be moderate fever. Loss of weight may be marked and cachexia may be present. The condition may resemble typhoid or tuberculous ulceration of the intestine, or ulcerative colitis of the idiopathic type. If the condition is present over a relatively long period stenosis is likely to occur, but even in this regard it cannot be distinguished from other varieties of ulcerative enteritis. Large hemorrhages may occur and this, in our case, was the probable immediate cause of death. Perforation with peritonitis may occur as a result of deep ulceration, with secondary infection from the bowel content. Death is the usual outcome, resulting from ileus, perforation or hemorrhage.

The clinical diagnosis must be uncertain as a rule. It will depend upon a wide correlation of clinical data. Given an ulcerative enterocolitis, or history of such with symptoms of stenosis, history of syphilitic infection with evidence of syphilitic lesion elsewhere in the body, and a positive Wassermann test, the diagnosis is strongly presumptive. It remains to eliminate, in so far as we can, other possible etiology and in the nonobstructive cases to await the results of specific therapy. The x-ray cannot be expected to give as much help as in gastric syphilis. Often the patient is too ill for such examination. A point of stenosis may be demonstrable in the small bowel. Except for the rather typical

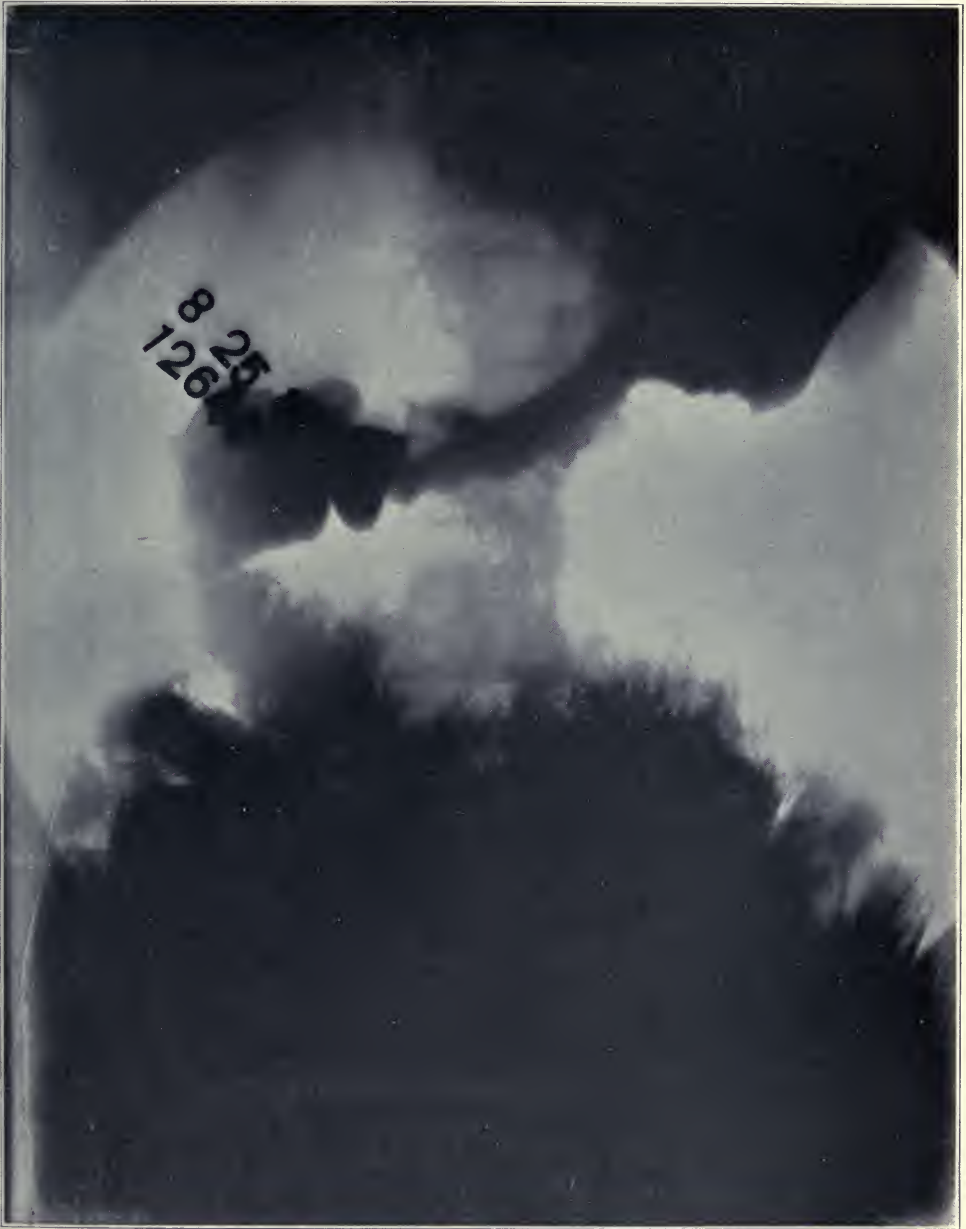

Fig. 1.—B. H., August 25, 1919, five minutes after barium meal.

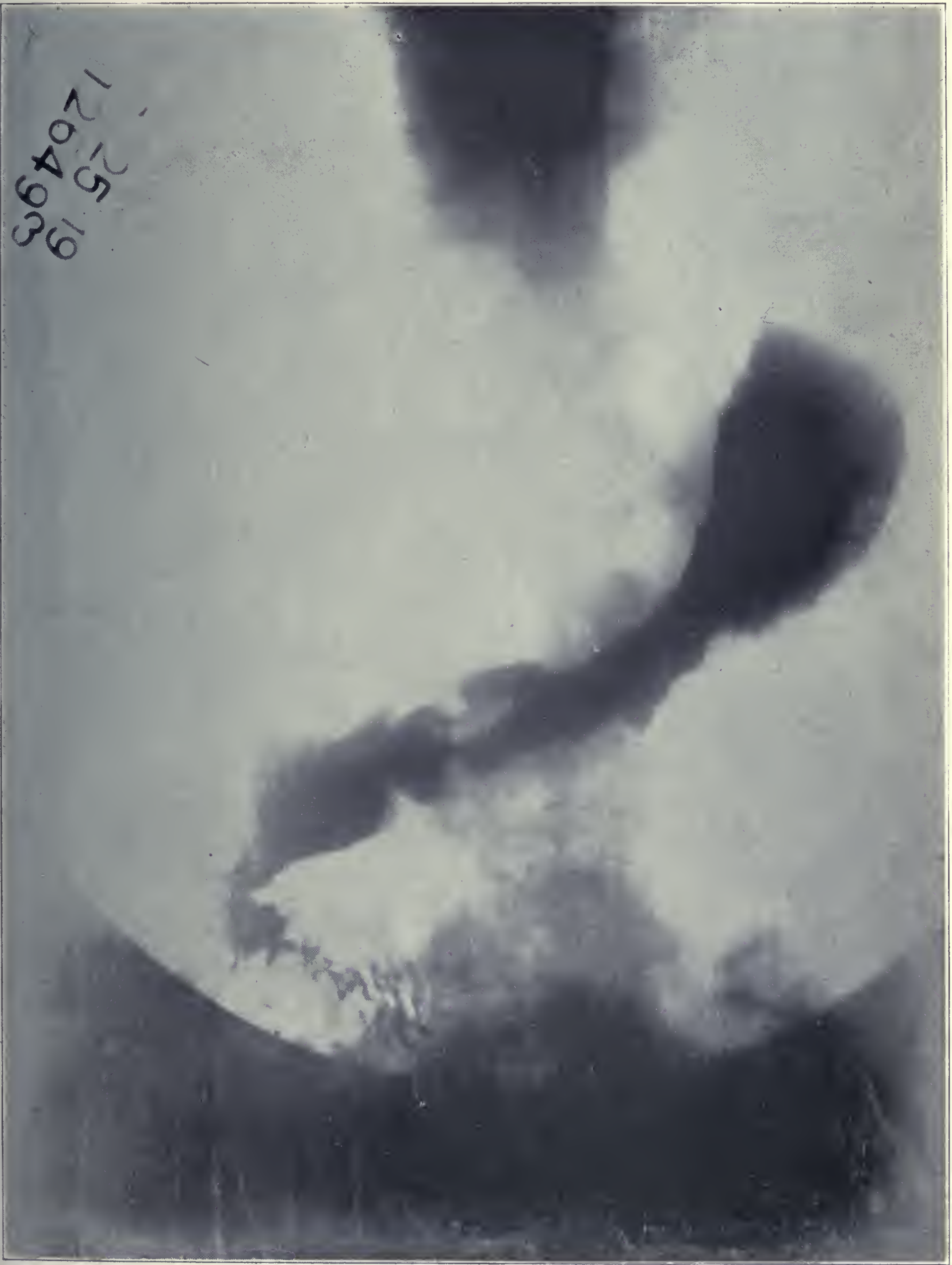

Fig. 2.—B. H., August 25, 1919, one hour and twenty minutes after meal.

long, narrow tubular smooth strictures, seen when the disease is confined to the rectum and sigmoid, the roentgen picture of lesions elsewhere in the colon can scarcely be distinctive.

Careful stool analyses are of importance to eliminate other causes of diarrheal processes incidentally occurring in syphilitics.

In a differential diagnosis we must consider carcinoma, tuberculosis, intestinal obstruction from various causes, adhesive peritonitis, typhoid fever, amoebic and other dysentery, and the ulcerative enterocolitis of the idiopathic variety.

The onset and course may be abrupt, complications and death occurring shortly, or the ulcerative process may be more or less intermittent and cases drag along for years (Riedel)[29] (Brunner).

In presumptive cases the antisyphilitic treatment should always be vigorously employed. The obstructive and tumor cases will require surgical interference.

Among 11,700 hospital admissions in this department there have been only three cases of syphilis of the stomach recognized. The routine serum Wassermann test has been applied to the last 8,500 admissions, the test usually being performed at the same time in two laboratories.

The clinical history of one of the three patients with gastric syphilis is given in considerable detail, because he was observed over three years, developed intestinal syphilis from which he died, and an autopsy was performed.

CASE.—B. H. (Medical 6674), white male; age forty-one; single, laborer; American born; entered the hospital August 24, 1919, complaining of ''stomach trouble.''

Social History.—Habits of eating and sleeping regular before present illness. Coffee three times daily. Alcohol to excess for ten years, ending twelve years ago. Admitted gonorrhea at twenty-five years but denied chancre.

Family History.—Unknown to patient.

Past Medical History.—Malaria at eight years. Frequent tonsillitis. He denied any general skin eruption. Six years ago he was struck with a piece of baling wire over the upper sternum, and the wound healed with a large scar. Respiratory and cardiac symptoms absent. Genitourinary history negative, except for the history of urethritis. He denied paralysis or paresis, ataxia, diplopia, lightning pains or girdle sensation. Slept well. Digestive system: Appetite usually good. No pain before or after meals, except an occasional attack of cramps and gaseous distress following heavy meals. No nausea or vomiting. Jaundiced for two or three days about five years ago, the attack associated with pain in the left epigastrium requiring a hypodermic injection.

Present Illness.—Began four years ago with cramping pains in the left upper abdomen, which lasted five to ten minutes and occasionally radiated to the right. The pain was usually associated with nausea and vomiting of a sour material. No pyrosis or heartburn. He had never vomited blood nor passed tarry stools. Bowels would be constipated. These attacks came on independently of food for six weeks, and then he felt fairly well until the latter part of May, 1919, when he had a similar attack following a period of constipation. No appetite for the past two months. He had noted since May that, when he had cramps in the stomach associated with gas, he often obtained relief by taking food or soda and described the pains as ''hunger pains.'' Lately from one to five times daily he had twenty minute spells of spitting water, occasionally with nausea. He felt hungry, but as soon as he tried to eat lost appetite and lived on milk for the past three months. He weighed 153 pounds in January, 1919, and now 111 pounds, the loss occurring chiefly in the past two months.

Physical Examination.—There were only the following points of interest: Well marked emaciation. A scar over the right frontoparietal region with depression in the bone. A 7 cm. flat scar over the menubrium. On examination of the abdomen only slight tenderness under the left costal margin, the abdomen flat without evidence of ascites or tumor, some increased resistance under the upper recti muscles. The liver and spleen were not palpable. The heart and lungs, pulse, respiration, temperature (throughout this admission), the pupils, reflexes and sensation were normal.

Laboratory.—Hemoglobin 70 per cent (Sahli). Erythrocytes 3,720,000. Leucocytes 7,800. Differential count normal. Serum Wassermann four plus. Gastric analysis 30 c.c. of contents removed at 45 min. Free acid O. Total acid 12. No occult blood. Microscopic examination negative. Stool analyses showed strong reactions for occult blood; the microscopic examinations negative. Urinalyses all negative. Roentgen examination revealed a filling defect occupying the greater part of the lower portion of the greater curvature and a marked dilatation of the duodenal cap. The stomach was completely empty at the end of six hours.

The patient was seen in consultation by the surgical staff and, though the Wassermann test was positive, an exploratory operation was advised and performed on August 30, 1919. ''Upper right rectus incision. A moderately firm regular mass was found to involve the fundus of the stomach, especially the posterior wall and the greater curvature. This mass was indefinite in its outline, and merged with the uninvolved stomach wall which was definitely thickened throughout. The mass was not globular but flattened, its longest dimension parallel to the axis of the stomach. It was not as hard or as irregular as most carcinomata, nor did it contain any area suggesting an ulcer crater. It did not encroach upon the pylorus. There were many palpable glands in the lesser omentum and some along the greater curvature of the

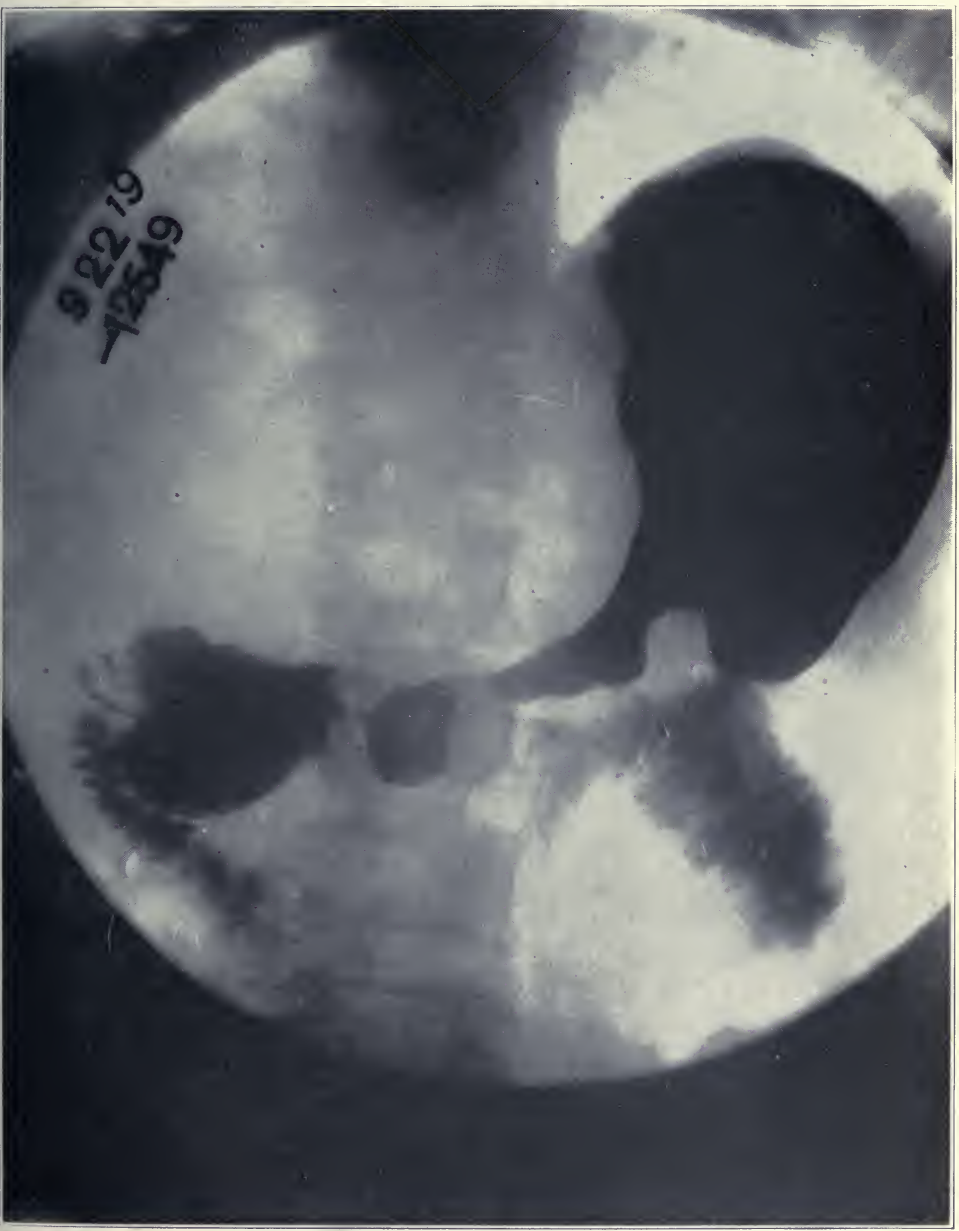

Fig. 3.—B. H., September 22, 1919, five minutes after barium meal.

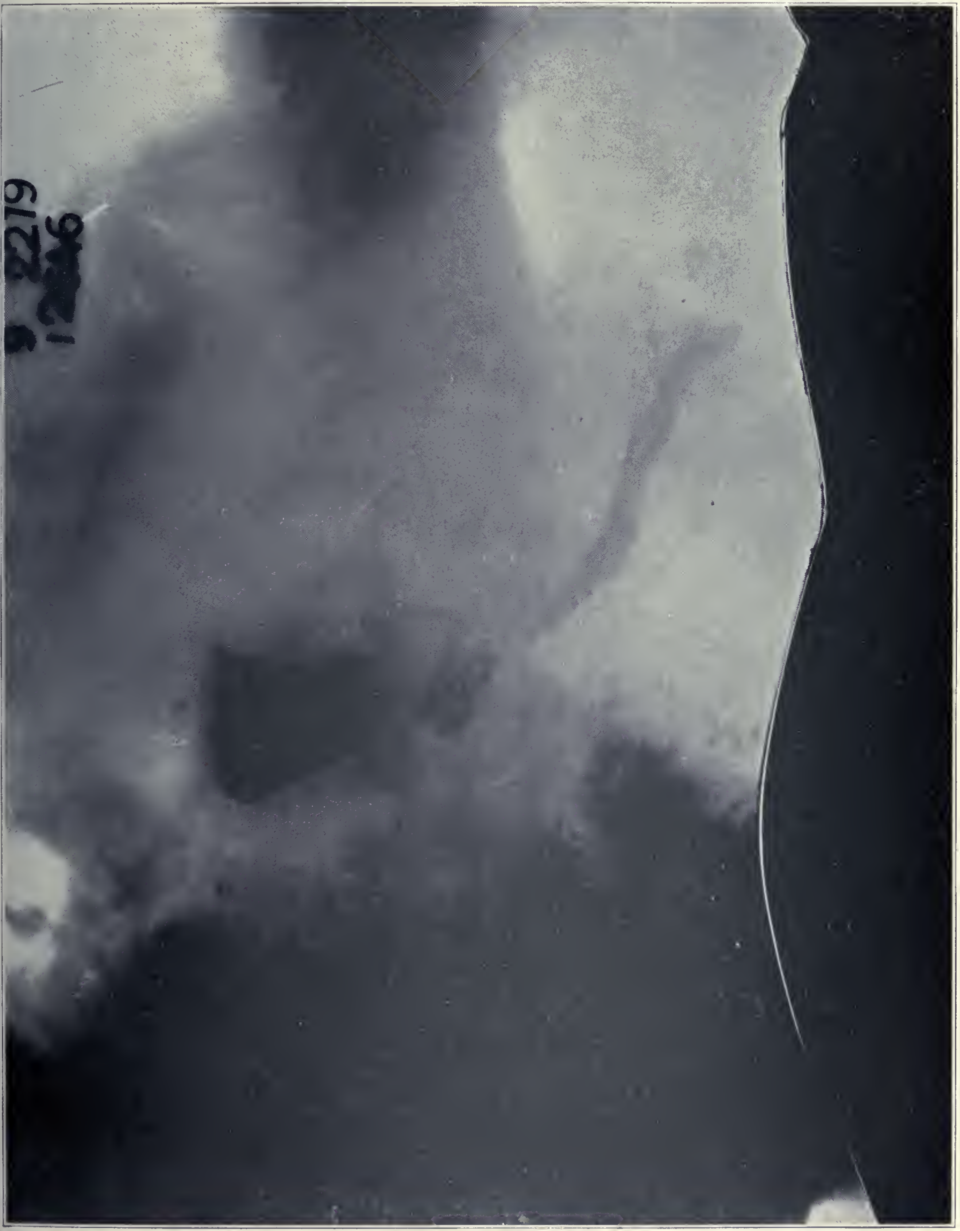

Fig. 4.—B. H., September 22, 1919, three hours after meal.

stomach, as well as some retroperitoneal, all softer than ordinarily associated with carcinoma, the largest split pea or bean size. There was an area between the under surface of the left lobe of the liver and the lesser omentum, which seemed to be infiltrated by a granular new tissue which bled very freely and required packing with iodoform gauze. The liver was lusterless, dark and definitely thickened, its free edge rounded. Its free surface presented several grayish white, slightly depressed areas, suggesting old scars. In view of the evidence of syphilis the diagnosis of gastric lues was made. If the condition was carcinoma it was inoperable, and there was no reason for doing a gastroenterostomy. (Dr. H. L. Beye).''

Histologic report (August 30, 1919) of omental lymph glands: Inflammatory lymph node.

On September 10 and 17 he received 0.6 gm. of diarsenol intravenously, in addition to daily mercurial inunctions and potassium iodide, grains 45, daily. He gained 8 pounds in the next four weeks. The x-ray on September 22, 1919, showed little or no change in the filling defect, and the emptying time was six hours. He was discharged October 1, 1919, with directions to continue the potassium iodide and mercury.

He was readmitted to the medical service on January 16, 1920, with the complaint ''inability to keep anything on his stomach.'' His appetite had been good. He suffered no pain. Vomited much of the food eaten, but might go two days without vomiting. Began work two weeks after discharge from the hospital, but unable to work for the past month. He had taken the mercury and iodide only irregularly, ''off and on.'' Gained to 126 pounds, and more than half of his strength. No vomiting of blood or food eaten the day before. No associated pain, nausea, or dizziness. He had often eaten a hearty meal shortly after vomiting. Food rarely present in the vomitus, even one-half hour after the meal. The physical examination was more negative than before. There was no abdominal tumor or tenderness, and the liver and spleen were not palpable.

Laboratory.—Blood. Hb. 81 per cent. Leucocytes 5,600. Erythrocytes 4,840,000. Blood smears normal. Wassermann four-plus. Ewald test meal after one hour gave 1450 c.c. of turbid fluid with bread crumbs and much mucus. Occult blood, three-plus. Lactic acid, one-plus. Free acid O. Total acid 36. Oppler-Boas bacilli, a few. Stools,—occult blood two to four-plus, but no red blood cells microscopically. A motor meal four days later showed no retention in twelve hours, but a motor meal three days after that showed, after ten hours, a retention of 275 c.c. with a good deal of mucus, no blood, free acid O, total acid 24. Urinalyses all negative. The x-ray examination showed about the same condition as previously. The pyloric sphincter and duodenal cap were well outlined, the stomach practically empty of barium in one and one-half hours.

Treatment.—The patient received three intravenous injections of diarsenol along with mercurial inunctions daily and potassium iodide increasing from 45 grains to 90 grains daily.

Nothing more was heard from the patient until October 4, 1922. He returned obviously very ill with the complaints of ''diarrhea and weakness.'' The interim history is negative except as follows: His appetite was fairly good until about September first, since then he does not care for any kind of food. Always constipated before his operation, since that time has had frequent attacks of diarrhea lasting as long as one to two weeks. In June, 1922, he began to have diarrhea and to get weak. Sometimes he would have six to eight stools a day. There was no pain, nausea, vomiting, tenderness of the abdomen or distention. He does not know if there has been any blood or mucus in the stools. There have been occasional periods when the diarrhea would cease for a few days or even a week, but he thinks that he has had diarrhea considerably more than half of the time. His strength has been steadily decreasing. Three weeks ago he had a temperature of 101°F. Since then it has oscillated between 99° and 102°, and he has been in bed the past two weeks because of weakness. No thin or ribbon-like stools. The patient admitted that he had taken no mercury or iodide since his discharge from the hospital. While the history was being taken the patient had a copious brown liquid stool with gross blood and mucus.

Physical Examination.—Considerable dyspnea, slight cyanosis and well marked pallor. Uvula and part of soft palate absent. Large septal perforation in nose. No enlargement of the superficial glands. No moisture in the lungs or any gross physical finding in the lungs. The heart was slightly enlarged to the left. Slight pulsation in the right upper front, slight diastolic shock at aortic area. A rough systolic murmur at the aortic area and a soft systolic murmur at the apex, the aortic murmur transmitted to the neck. No diastolic murmur. Radial pulses equal and synchronous. Blood pressure 126-60. Pupils equal. Abdomen distended, a little resistance at the upper end of the scar. Edge of liver could not be definitely felt; no hepatic tenderness. Spleen readily felt and tender. No other abdominal tenderness and no palpable tumor mass. Digital examination of the rectum was negative. A proctoscopic examination was not made because of the acute illness.

Laboratory.—Blood Wassermann four-plus. On October 4, 1922, the Hb. 80 per cent; red cells 4,350,000; leucocytes 3,700 with 80 per cent polymorphonuclear neutrophiles and 20 per cent lymphocytes. The following day leucocytes 2,550 and on October sixth leucocytes 4,800 and red cells 3,640,000. Stools: Three stools examined on October sixth were free from occult blood, pus and mucus and ameba. Two stools on October eighth were liquid, with much gross blood and large clots. Urinalyses showed a little albumin, a few pus cells, and no casts or red blood cells. Sputum examinations done almost daily showed no tubercle bacilli. Agglutination tests with the serum gave a negative Widal reaction for typhoid and paratyphoid. A blood culture was negative.

The temperature on admission went to 104° but dropped to subnormal in twenty-four hours and was very irregular after that, ranging between normal and 102.4°. The respirations ranged between 20 and 26 per minute, and the pulse 90 to 116. Stereoscopic plates were taken of the chest and these showed no evidence of tuberculosis nor aneurysmal shadow. A barium enema was not given because the patient was too ill, and because of the hemorrhages from the bowel. He was delirious at times. Potassium iodide was given, 45 grains a day for three days, then 90 grains a day.

On October 10th at 6 P. M. he experienced abdominal cramps, called for a bed pan and passed from a half to three fourths of the pan full of liquid blood

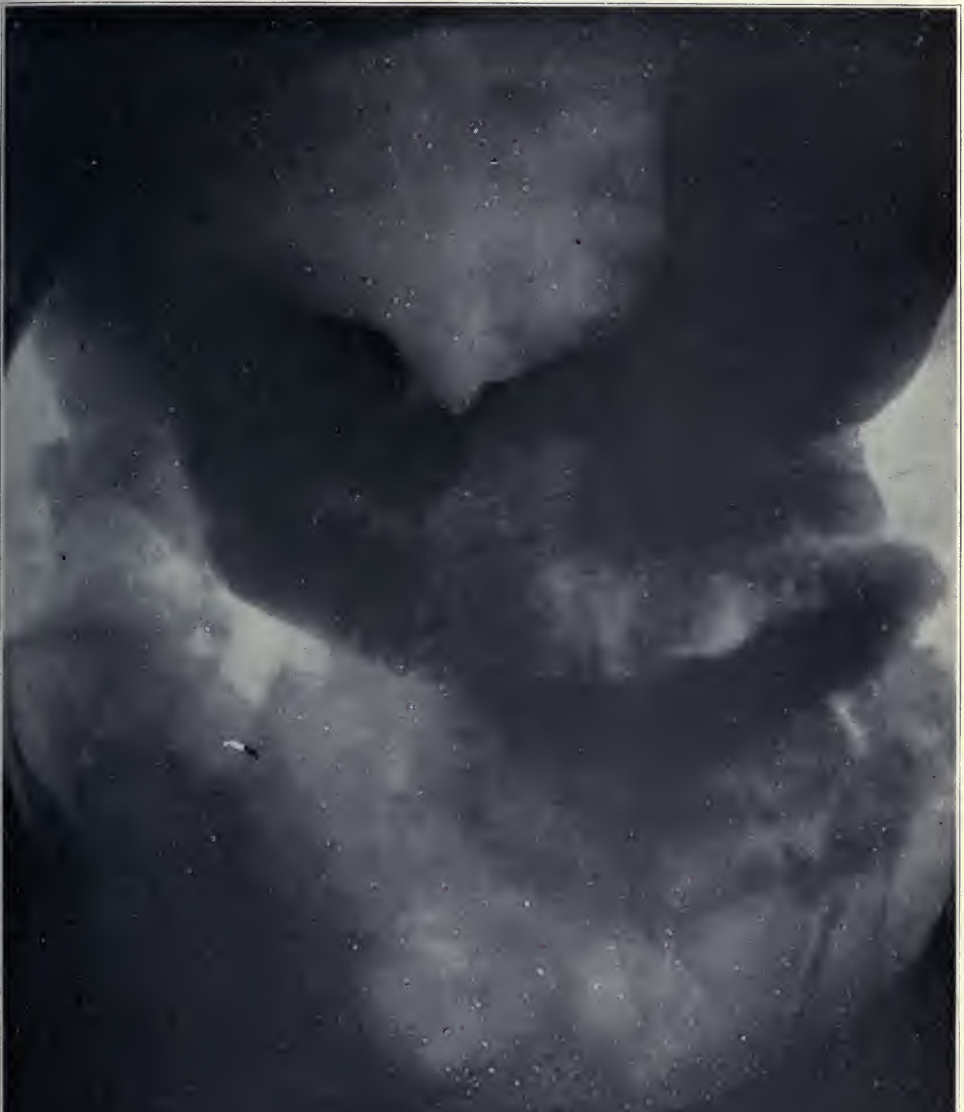

Fig. 5.—B: H., January 16, 1920, five minutes after barium meal.

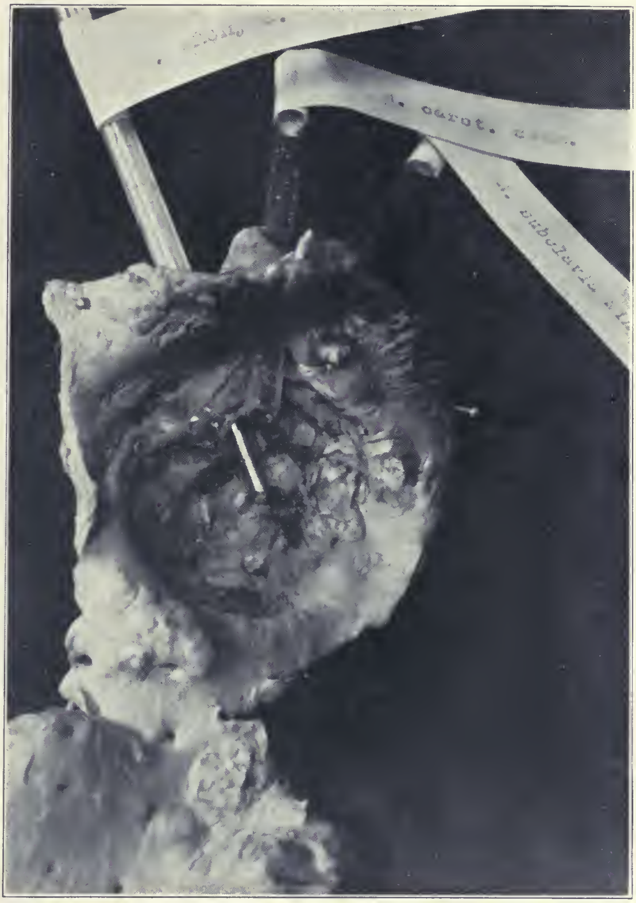

Fig. 6.—Aneurism of the aortic arch.

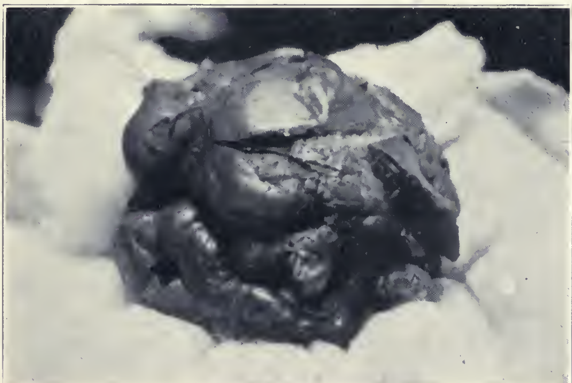

Fig. 7.—Liver, inferior aspect.

and clots. Weak and exhausted afterwards. Four hours later he was transfused with 500 c.c. of citrated blood. He died at 9:20 the following morning.

Only such parts of the protocol as bear on the subject of the paper are given in particular. All the other interesting facts of the protocol are mentioned briefly.

Gross Findings.—An autopsy of the head was not obtained. There are no marked pathologic changes of the organs of the neck and thorax, except of the aorta. No changes are noted also on the extremities and none of the genitourinary tract. The aorta shows very prominent chronic mesaortitis, with the formation of aneurysm the size of a hen's egg in the upper part of the ascending portion. The liver is a typical hepar lobatum or gnarled liver. The spleen is greatly enlarged (640 gm.). The stomach shows what we call a leather-bottle form. The entire organ is altered, but beginning about 2 cm. proximal to the pyloric ring and extending toward the cardia for 6 cm. the entire wall is about twice as thick, (8 mm.) as the remainder of the stomach, which is a little over 4 mm. thick. It is firm and of uniform consistency with all parts involved alike. The mucosa has lost its velvety appearance and feels firm and indurated. There are no ulcerative lesions of the mucosa. There are no changes in the duodenum, jejunum and ileum to 120 cm. proximal to the cecum, where ulcers of the ileum appear. There are about a half dozen in the ileum and many more in the large intestine. They finally disappear in the distal portion of the sigmoid. The ulcers vary in size, the largest being 5 x 1 cm. but their shape and position are always the same. They are elliptical, the long diameter perpendicular to the intestinal axis. The floor of the ulcers is always below the level of the mucosa, but not deeper than 2 mm. The margins of the ulcers are distinctly indurated. They are in different stages so that it is possible to follow up their gradual development: (1) a very small and superficial defect of the mucosa; (2) the bottom of the mucosal defect sloughed and a complete ulcer formed; (3) the ulcerated bottom is cleaned; (4) repair of the ulcerated mucosa has begun and finally; (5) a circular scar in place of the former defect (one place).

In no place have we seen any dependence of the site of the ulcer upon the Peyer's patches. In two places corresponding to ulcers of intestinal mucosa there are recent blood-stained fibrinous adhesions, one between the ileum and parietal peritoneum, and one between the ileum and fundus of the urinary bladder. There is no actual perforation of the intestine. The mesenteric glands are slightly enlarged, the sectioned surface flesh color, without any evidence whatever of necrosis.

MICROSCOPIC FINDINGS.—LIVER.—There is a prominent increase in fibrous tissue in the portal spaces. The increased fibrous tissue extends into the lobules. Occasionally we find endarteritis with numerous round cells infiltrating the surrounding tissue. The liver cells in the neighborhood of the fibrous tissue are partly separated from each other by this exuberant tissue so that in some portions the changes resemble pericellular cirrhosis.

Spleen.—Chronic interstitial splenitis.

Stomach.—The mucous membrane is replaced by connective tissue with wide capillaries, and in this tissue there is a very abundant diffuse cellular infiltration. Here and there we still find gastric mucosa elements, which have lost their definite characteristic relationship to each other. The infiltrating cells are very small, round, with very scanty protoplasm and deeply stained around eccentric nuclei. These cells never show epithelioid or giant cell characteristics. The submucosa is infiltrated to a lesser extent. The muscular layers of the wall do not show any marked pathologic changes. Notwithstanding the diffuse infiltration of the mucosa we are still able to note numerous cell conglomerations. These groups are very prominent in the submucosa, are perivascular and more or less round. There are no necrotic changes in the stomach wall. There is a well-marked excess of interstitial connective tissue of the muscular layers.

Intestines.—The mucosa surrounding the ulcers is entirely replaced by connective tissue supplied with numerous wide capillaries. This tissue is diffusely infiltrated with numerous small, round cells which have deeply stained round nuclei and almost no protoplasm. These infiltrating cells are so numerous that it is difficult to distinguish the histologic elements of the intestinal wall. The submucosa is also infiltrated with cellular elements of the same type, but the greatest changes are found here in the vessels. The diffuse infiltration of the mucosa and submucosa disappears in the muscular layers. In the wall of the ulcer this infiltration is gradually replaced by masses of fragmented nuclei, remnants of protoplasm and small round cells. The bottom of the ulcer is formed by the submucosa. The more complete the destructive process, the more prominent is the infiltration of the adjacent tissue, and vice versa. In general, the submucosa is distinctly thickened and very interesting changes in the blood vessels are noted. We see there, as a rule, obliterative endarteritis. Tissue rich in spindle cells appears between the elastica interna and the endothelium lining the intima. We find similar changes also in the veins. The adventitia and the muscularis are infiltrated with numerous small, round cells of the same appearance as that described above. These cells we find only in the veins. This affection of the vessels is not always found in arteries and veins of the same section. We find places where the veins are relatively normal, while arteries are markedly affected and vice versa. Such changes are not universal throughout the entire length of such affected vessels, but are rather regional. We are convinced of this fact by examining a series of sections from the same block; affected portions of vessels follow those that are little or not at all involved. The best way of examining these exceedingly interesting proliferative changes in vessels is by the use of Wright's elastic fiber stain. With this staining method we have been able to establish that the vessels of the submucosa are almost entirely destroyed through the cellular infiltration and other proliferative changes in their walls. Often only the circular elastic fibers remain to mark the location of the previous vessel.

Such are, briefly, the most important facts of our study of this case. We will turn now to the establishment of the diagnosis through the interpretation of these facts. What diagnosis is suggested by the above described changes in the stomach? We have here a chronic, general diffuse involvement of the stomach wall with formation of connective tissue, causing shrinkage of the stomach. Such cirrhotic changes we meet with in two conditions: in

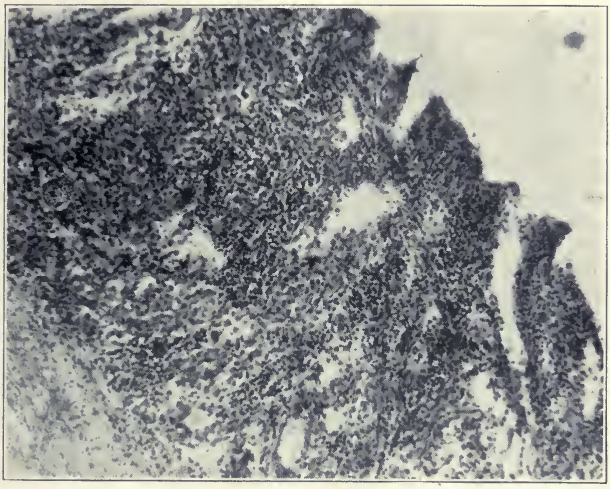

Fig. 8.—Showing the changed mucosa of the stomach.

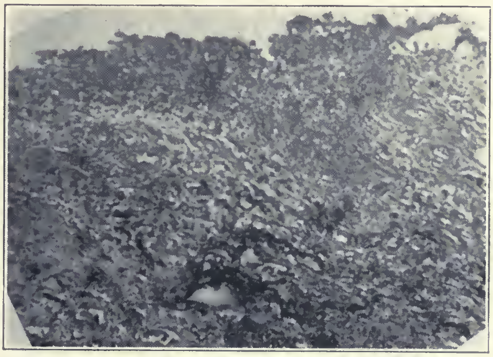

Fig. 9*A*.

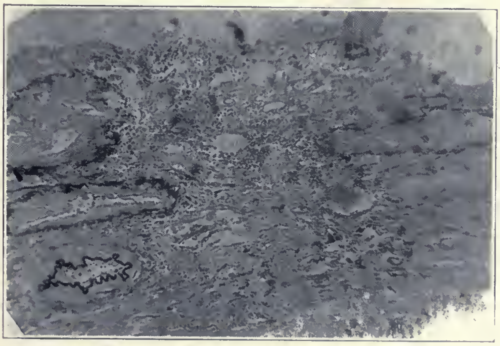

Fig. 9*B*.

Fig. 9.—Two adjacent serial sections of the edge of the ulcer from the small intestines. *A*, Hamatoxilin-Eosin stain. *B*, Weigert's elastic stain.

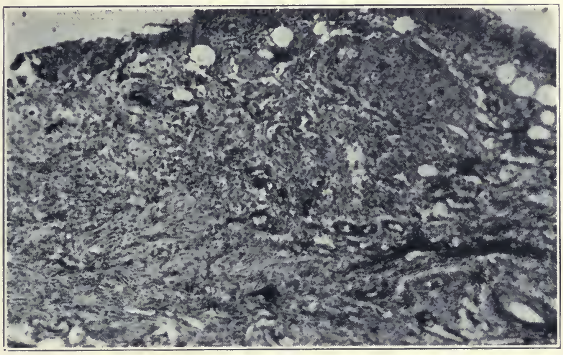

Fig. 10*A*.

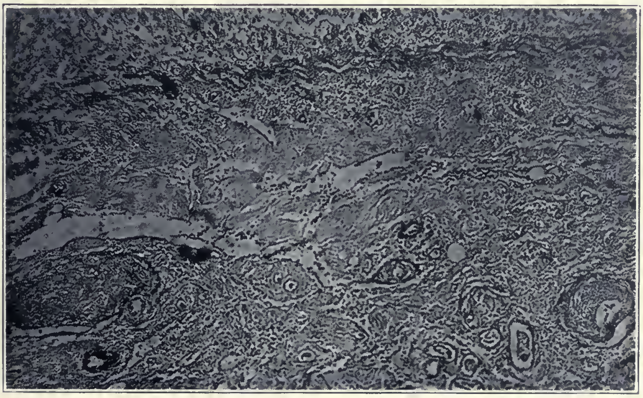

Fig. 10*B*.

Fig. 10.—Two adjacent serial sections of the edge of the ulcer from the large intestine. *A*, Hamatoxilin-Eosin. *B*, Weigert's elastic stain.

the very rare tertiary involvement of the stomach in acquired syphilis, and in linitis plastica. The very complex changes in the blood vessels and the perivascular infiltration speak against linitis plastica in this case, and for syphilis. The gross findings of the intestine lead us to consider (1) typhoid fever, (2) tuberculosis, and (3) syphilis. The absence of any dependence of the site of the ulcers upon the Peyer's patches, and the entire absence of any evidence of typhoid fever in the patient's history are sufficient to exclude the possibility of this condition. It is not so easy to exclude tuberculosis, especially if we take account of Fibiger's opinion that most cases described as syphilis of the intestine are really tuberculous. In our case the gross appearance itself speaks against tuberculosis. We do not see the typical ringworm shape of the tuberculous ulcer with the sinuously undermined, dentated edges, and grayish yellow nodules on the base and margins of the ulcer. Further, if we should admit here a tuberculous involvement of the intestines we would have to do with a primary tuberculous affection, because of the absence of tuberculous changes in the lungs and other organs which could give rise to a secondary involvement. Such primary tuberculous involvement of the intestines is very rare in general, and entirely unlikely in persons of the fifth and sixth decades. The fact that the mesenteric lymph nodes do not show any caseous necrotic changes speaks against tuberculosis. We understand that tuberculous adenitis can be present in lymph glands which do not show all the classical signs of tuberculous involvement, or even any hyperplastic changes (Orth), but these are rare, while in our case with such an extremely vivid process with numerous ulcers we would expect a complete typical involvement of the glands. Finally a careful search for tubercle bacilli was negative. All these considerations force us to exclude tuberculosis. The gross and the microscopic findings of the stomach and intestines, in association with other gross evidences of visceral syphilis, lead to the diagnosis of gastrointestinal syphilis. The obliterative endarteritis in the stomach and intestines is not exceptional, and is found not only in syphilitic involvements but also in other chronic conditions, but the changes described in the veins and also the perivascular cellular infiltration surely are striking signs of the so-called phlebosclerosis syphilitica. The typical syphilitic lesions of the aorta and liver confirm the diagnosis. The changes in the stomach and intestines are of primary importance as a classical example of acquired syphilis of the digestive organs.

The great discrepancy between the numerous reported cases of clinical syphilis of the stomach and intestines, and a few diagnosed from the histopathologic findings is explainable by the fact that various authors interpret differently the essential findings of the pathologic conditions of the digestive organs. While pathologists admit syphilis only in cases which have been verified histopathologically, other authors establish the diagnosis on the so-called specific clinical symptomatology, a positive Wassermann reaction, and the results of antiluetic treatment. The rarity of syphilis of the stomach and particularly of the intestine speaks against any known typical clinical symptomatology of these conditions. The highly subjective element in the evaluation of the results of specific treatment, in each instance, renders the results of therapy only of doubtful importance in the differential diagnosis. Moreover, in the clinical series reported by Smithies antiluetic treatment freed the patients from symptoms of dyspepsia in only five out of thirty-five cases in which the diagnosis of syphilis of the stomach was established largely from a positive serum reaction. It is clear, therefore, that all of the reported cases of syphilis of the stomach based only upon the "clinical symptomatology," Wassermann reaction, and results of antiluetic treatment are not at all convincing. Even the microscopic diagnosis of these conditions is very difficult. The microscopic proof of the diagnosis by finding spirochetes in the tissues is practically hopeless as we see from the work of many authorities (Crowell, Aschoff, Symmers). Eustermann states: "After all, there is no decisive, ultimate diagnosis because, to the present time, spirochetes have not been demonstrated in the tissue and we know that histopathologic criteria are not conclusive." We cannot agree with this. Recently McNee has been able to demonstrate spirochetes abundantly in an actively developing submucous gumma of the stomach. However, this condition will be rarely seen by the pathologist in such stage of its development. We are, as a rule, unable to demonstrate the spirochetes, but still we know a series of highly interesting peculiarities of the histopathology which help us to differentiate this condition with almost exceptional exactness. The small cellular infiltration is one of these peculiarities. The uniformity of the nuclei shows us that these cells do not belong to the leucocytes. I do not mean to say that the presence of these cells is specific, but they have a typical relation to the tissues, and especially to the vessels, with their insubordination and lack of respect towards the surrounding tissue. Moreover, these cells do not involve the vessel wall along its whole extent, but only in parts; this seems to be a somewhat characteristic peculiarity of the syphilitic poison. Finally, the so uncharacteristic granulation tissue which leads to infiltration and, afterwards, to the disintegration of the digestive tube, also speaks for syphilis. All these peculiarities are so characteristic that we are usually able to establish our diagnosis on account of them.

These are the reasons for considering that only those cases of syphilis of the stomach and intestines which have been diagnosed histopathologically are absolutely convincing.

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PARALYSIS OF THE SEVENTH CRANIAL NERVE IN EARLY CONSTITUTIONAL SYPHILIS

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San Francisco, Calif.

(Received for publication, October 8, 1923.)

IN such a highly neurotrophic disease as syphilis the coincidence of a paralysis is always of interest, and the patient whose history we are about to relate furnished quite a startling example of this conjunction. The man consulted us on a Saturday afternoon, suffering from a pronounced florid syphilis. On the following Monday in addition to his chancre and eruption, he had developed a well marked Bell's palsy, without, as far as we could ascertain, any other than his treponemal infection to account for its occurrence. For instance, there was no exposure to a cold draft which is so frequently present in the history of this affection as to give rise to the epithet "a frigore."

A man, thirty-eight years of age, consulted us November 18, 1922, on account of an eruption which he thought was a more general outburst of an eczema for which we had previously treated him. It was a typical luetic roseola, and the chancre which the patient had regarded as a trifle was typically Hunterian, situated in the sulcus. He had been exposed five weeks previously, and the chancre had been present two weeks. There was right inguinal and posterior cervical adenopathy.

This call was late on a Saturday, and the initial treatment was deferred until Monday, and when he appeared for treatment on Monday afternoon he had a paralysis of the left facial nerve, which he had first noticed that morning. The paralysis, therefore, antedated any antiluetic treatment whatever. It was, therefore, either due to the neurotrophic luetic virus or was a coincident Bell's paralysis of unknown etiology. On calling again, five days later, he said that he had noticed for the past few days some deafness of the left ear, and there was tenderness over two points, one over the malar bone and the other over the inferior maxilla. The deafness was never more than a slight decrease in the acuteness of hearing.

The paralysis involved the muscles of the forehead, eyelids, cheek and mouth, supplied by the seventh nerve. It, as indicated above, came on suddenly, and then very slowly improved until now, after 9 months, it is almost entirely unobservable. The steady antiluetic treatment with both arsphenamine and mercury had not had the slightest apparent effect upon it.

Dr. Eugene S. Kilgore took an active interest in the case because of the rapid evolution of the malady. He thinks that in such cases the aorta is early affected. A skiagraph showed only a suspicion of this condition with no corroborative clinical symptoms.

Because of the strongly neurotrophic tendency of the syphilitic virus a Bell's palsy occurring in the florid stage may be attributed to it. When there is bilateral paralysis accompanied by paroxysmal nocturnal pains it is almost certainly caused by it. A meningitis or a periostitis affecting the cranial foramen of exit may also cause such a paralysis. But these lesions usually occur at a later stage of syphilis, and we have no reason to suspect their presence in this instance. And furthermore, these palsies recover remarkably swiftly, which was not the case here.

We would, therefore, report this case as occurring in early syphilis. As no other traumatism or infection was found to be present, it might be inferred that it was luetic.

It was fortunate that the paralysis occurred previous to the administration of the arsphenamine, as otherwise we might have thought that the drug had influenced the occurrence of the paralysis, and therefore, might lead, if persisted in, to even more serious disease of the nervous system. Incidentally, we may remark that we have never seen evidence showing that the administration of arsenobenzol causes increased incidence of neural syphilis.

HEMIANOPIA AS THE SOLE CLINICAL FEATURE IN UNTREATED SECONDARY SYPHILIS

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It is well known that cerebrospinal implication in syphilis is an early manifestation and not, as was previously taught, a "tertiary" phenomenon. Its obvious clinical exhibition, however, is not always apparent. Many workers have shown that the majority of cases of syphilis in the secondary stage, and many in the primary stage, show definite biologic and cystologic evidences of intrathecal involvement.

It is highly probable that generalization of syphilitic infection has occurred before the chancre appears. The experimental work of Metchnikoff and Roux, Neisser, Brandes and others has proved conclusively that the localization of the spironema does not exceed twenty-four hours. Any local evidence of reaction to the invader does not appear for an average period of twenty-one days. During this time lymphatic and vascular spread of the parasite has been taking place, but at what rate we can only surmise. We know, however, that when local reaction occurs and the chancre appears at the point of entry, generalization has advanced so far that local destruction or excision of the chancre is unable to modify or abort the disease. Already all tissues are equally accessible to the parasite. It follows then that the first tissue to be attacked is that which affords the most favorable conditions for proliferation and growth of the spironema. The first tissue to show clinical evidence of such attack is that which possesses the lowest powers of resistance, which is so situated that it receives the greatest flood of spironemata, and which is most susceptible to damage and capable of showing clinical evidence of such damage.

There is a good deal of evidence to show that the spironema in the new host flourishes best in the tissue from which it originally was derived. This conception has led to the differentiation of spironemata into two distinct strains—the one dermotrophic and the other neurotrophic. It has been stated that these strains can be differentiated morphologically, but this is not generally accepted. Such differentiation into strains, therefore, is based on clinical observations.

In the cerebrospinal axis the Spironema pallidum has no exclusive site of attack. This we would take for granted were we to consider the all important fact that the mode of dissemination of the spironema is one of vascular and lymphatic spread. Moreover, these structures are subjected to grave attack during the process of this dissemination. Syphilitic septicemia is exhibited by pyrexia, headache, malaise and so on, frequently long before the surface evidence of so-called secondary syphilis is apparent. We have no reason to expect that the cerebrospinal axis should escape during this period of septicemia. We should therefore expect the disease in the central nervous system to be essentially one of lympharteritis, and this histologic study proves to be so.

It is a fact, however, that a dominating cerebral manifestation in the early stage of syphilis is an occurrence of much rarity. Even in cases where the infecting strain of spironema is believed to be neurotrophic the earlier manifestations, with the exception of serologic and cystologic changes, usually are absent. This may be due to the fact that disease of the lymphatics rarely betrays itself by clinical symptoms. Where the strain is not considered neurotrophic *sui generis,* any cerebrospinal manifestations usually occur while the cutaneous lesions are still in process of evolution or resolution.

In these days of salvarsan therapy of syphilis, meningeal irritation and the so-called ''neurorecidives'' have received much attention. These curious manifestations of neurosyphilis vary from a mild clinical variety including headache, insomnia, tinnitus and vertigo, through the characteristic implication of individual cranial nerves especially the second and eighth, to a severe type which exhibits such symptoms as mental confusion, epileptic fits, dementia and even coma. They are partly meningolymphovascular and partly parenchymatous. The generally accepted explanation is that they are precipitated by interference with antibody supply resulting from inefficient massive-dose salvarsan therapy. Spironemata are destroyed very suddenly, and an intense local inflammatory reaction occurs in the immediate neighborhood. Endotoxins are released which attack the brain or meninges producing a neurorelapse. By pushing salvarsan further the remaining circulating spironemata are dealt with and the lesion disappears. Such neurorecidives are by no means rare, but their incidence is always subsequent to the administration of salvarsan or its derivatives or substitutes. Such an isolated lesion must not be confused with a nurosyphilide occurring in the early stage of syphilis in the absence of salvarsan therapy. Such a neurosyphilide is uncommon. For this reason we consider the presentation of the following case justified, particularly on account of the fact that the ocular lesion was the sole clinical evidence of systemic disease at a time when one would have been expected to search the skin and mucous membranes for signs of luetic activity.

In syphilitic lesions of the cerebrospinal axis we recognize two distinct classes. The first is a meningolymphovascular type which includes gummatous and endarteritic processes. Pressure symptoms from large gummata invading the brain and cord are well known. These arise from nonnervous tissues. Diffuse gummatous infiltrations may occur in the meninges or blood vessels of the cerebrospinal axis. Endarteritis culminates frequently in thrombosis of the affected artery resulting in an infarct in the brain or cord followed by corresponding sclerosis. The second class is one of parenchymatous nervous disease characterized by primary degeneration of specialized nerve cells and nerve tracts. For this class of disease the direct action of syphilitic toxin upon the nervous structures is responsible. Sclerotic overgrowth of the neuroglia in the affected areas may follow primary degenerative lesions, quite independent of any gross meningeal, lymphatic or vascular lesion. Examples of this group are found in dementia paralytica, tabes dorsalis, Erb's syphilitic paraplegia, and certain forms of primary optic atrophy. The important difference between these two groups lies in the prognosis. In the first class prognosis is good whereas in the second class prognosis is always relatively bad;—at the most we can hope to arrest the process, but we cannot attempt to produce anatomic repair.

Hemianopia is by no means a rare manifestation of syphilitic meningeal affection. It may be found in those cases where the optic radiations are affected, the lesion occurring anywhere between the chiasma to the occipital lobes. This symptom, however, is usually a late one, due to endarteritis, perivascular infiltration and gummatous changes.

In specific basilar meningitis the cranial nerves are rarely individually affected. As a rule the several cranial nerves situated in close relationship anatomically are involved simultaneously. Oscillating hemianopia (hemianopia fugax) has been described as being characteristic of basilar syphilis.

The optic nerve is usually secondarily affected—that is to say, there is no primary affection of the nerve substance itself, but changes are produced by extension from the meninges. Certain forms of primary optic atrophy, however, belong to the toxic parenchymatous group. By far the most common lesion is compression by gummatous proliferations or infiltrating meningitis. Such changes as choked disk, optic neuritis, irregularities in the field of vision, scotomata, optic atrophy and so on, are well recognized as being late luetic stigmata.

REPORT OF A CASE.—The patient, H. P., an unmarried European of twenty-nine years of age, developed a hard chancre on the left side of the glans penis in the latter part of October, 1921, in East Africa (Mombassa). This sore healed without treatment of any kind in eight weeks' time, and, being a long distance from medical aid, he received no treatment. He had no other evidence of syphilitic infection. Being an educated man, however, he was uneasy concerning his infection and, arranging for leave forthwith, came to Cape Town on February 14, 1922. He stated that the sore was his only symptom until, coming along the African coast, he thought his vision was not so good as it had been when he left Mombassa. By direct questioning (A. W. S. S.) it was ascertained that he first noticed a ''film'' before his eyes toward the right side not more than two weeks previously. When reading he had to turn his head to the right in order to see words at the ends of the printed lines. There was no other complaint, ophthalmic or otherwise. A recent large indurated scar was apparent on the glans penis. Adenopathy was general. There was no skin or mucous membrane lesion of any kind, old or recent. Examination of the central nervous system revealed no abnormality whatever apart from the eye condition. The serum Wassermann reaction was ++++ (four plus), the serum fixing the maximum number of M. H. D.'s of complement. The patient declined to have his spinal fluid examined.

On ophthalmic examination (2/17/22) the following data were obtained:

Visual Acuity: R. V. 5/36. L. V. 5/5 partly: under cycloplegia (homatropine and cocaine) R. V. with 3.00 sph. = + 1.00 cyl. ax. 20↙ = 5/24. L. V. with + 0.50 sph. = 5/5 partly.

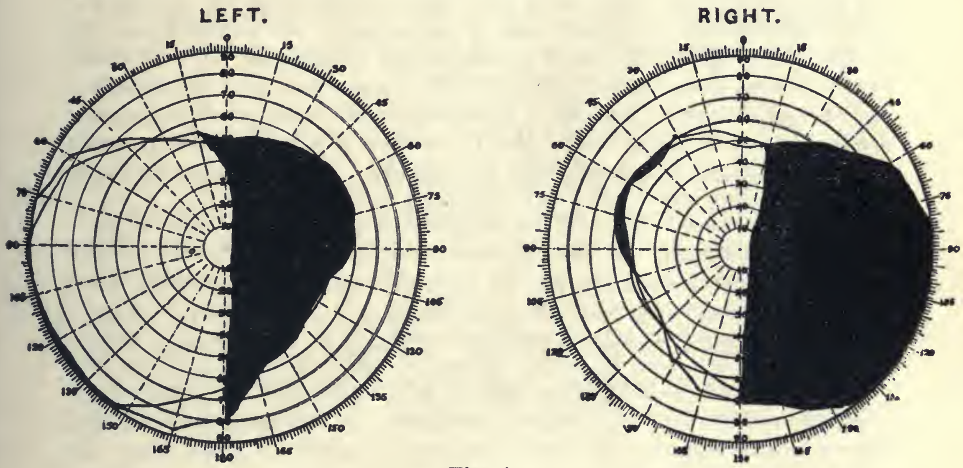
Accommodation: Punctum Proximum. R = 17 cm. L = 14 cm.

Muscle Balance: Orthophoria at 4 meters. 12° exophoria (varying) at 33 cm.

Tension: R. and L. normal.

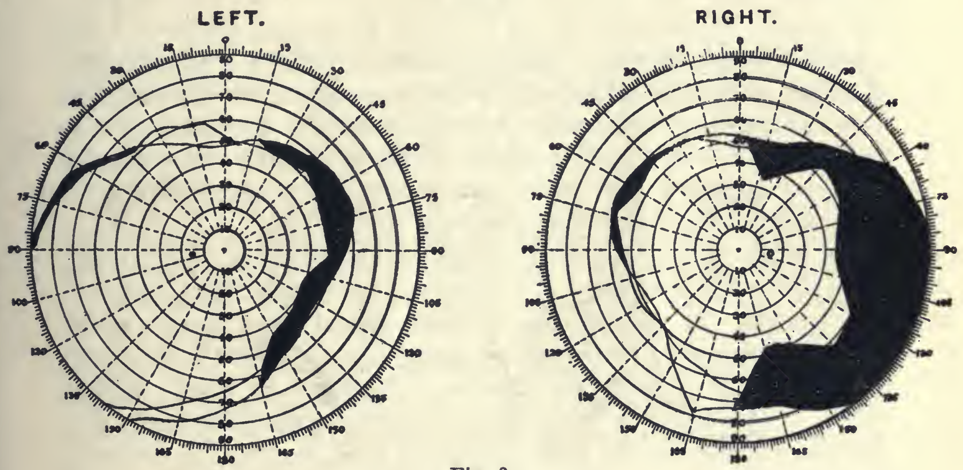
Pupils: These were regular in contour, equal in size, and reacted briskly to light, direct and consensual, and to accommodation-convergence. Wernicke's hemiopic reaction could not be elicited.

Fundi: There were no pathologic changes present.



LEFT. RIGHT.

Fig. 1.



LEFT. RIGHT.

Fig. 2.

Ocular Excursions: These were unimpaired in the six cardinal directions. No diplopia was elicited by the candle test, and there was no nystagmus.

Lids: Movements were full and strong, and there was no ptosis. The left palpebral aperture was slightly smaller than that on the right side.

Corneal Sensibility: This was not impaired on either side.

Fields of Vision: There were no central color scotomata. Perimetric charts (Fig. 1) showed complete loss of vision in the right half of each field, the line of demarcation passing to the right of the fixation point.

Treatment was instituted immediately, but on account of the fact that the patient lived some 30 miles out of Cape Town, it was found impossible to arrange the therapy which one would have liked. Moreover his leave was limited, and specific arsenobenzene treatment could not be pushed to its furthest limits. He received, however, 1.95 grammes novarsenobenzol intravenously in four weeks, spread over ten doses (2/14/22 till 3/17/22). Larger doses were not considered indicated on account of the risk of damaging nervous tissue which had already proved itself to be susceptible to attack. Mercury was administered by mouth in the form of pil. Hg. protoiodide, gr. 1/3, t.i.d. This he was instructed to continue for three years, twenty-one days per month.

Precisely one month after the previous perimetric reading, the fields of vision indicated a recession of the blind area to approximately the 50° circle: i. e., a relatively complete recovery in the left eye, and more than half the full extent of the normal field in the right eye. (Fig. 2).

No other systemic or nervous symptoms developed in the meantime. On account of force of circumstances he returned to East Africa on 3/18/22. The publication of this note has been delayed in the hope that the patient might reappear in Cape Town for further observation and treatment, but this hope has not been realized.

COMMENT

From the ophthalmic standpoint the case resolved itself into one of a right-sided homonymous hemianopia as the sole pathologic feature. The complete absence of systemic syphilitic manifestations is particularly striking. The slight difference in size between the palpebral apertures may have been congenital, or possibly due to sympathetic irritation though proptosis was absent.

The lesion present would be left-sided, and situated at any point along the optic tract from the chiasma to the subcortical and cortical centers. In the absence of other clinical signs there was no means of accurately localizing the point of interference with visual perception excepting the significance of the hemiopic pupil reaction which, in this instance being absent, would suggest that the lesion was not situated in the optic tract at a point anterior to the spot where the fibers to the oculomotor nucleus are given off.

REMARKS ON VISCERAL SYPHILIS

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THE interesting paper, "Unsuspected Syphilis," which appeared in the New York Medical Journal, September 5, 1923, from the the pen of Dr. Loyd Thompson, has incited me to offer this small contribution on the subject. Syphilis of the nervous system is, at present, too well known to elicit comment, and this likewise applied to the cardiovascular apparatus, since the specific etiology of many of its morbid processes has for some years been a clinical and therapeutic acquisition. Therefore, the pulmonary, gastric, hepatic, and renal manifestations of lues alone will be considered.

After much discussion, it would now clearly seem that the lungs are frequently specifically involved by the treponema. Many observers have regarded this as infrequent, but probably it has been considered as uncommon because of diagnostic difficulties existing in the past. The clinical types to be considered are those of the secondary and tertiary phases of the infection.

In the secondary phase there is, first of all, the early tracheobronchitis occurring during the secondary septicemia, and simply indicating the presence of an enanthema of the respiratory mucosa. Symptomatically, there is paroxysmal coughing while auscultation reveals some sibilant râles. It is accompanied by anemia and asthenia, while the vulgar secondary lesions, if present as is usual, render the diagnosis self-evident. But stress should be laid on the fact that should this bronchitis assume some clinical importance, it is an index of severe luetic infection.

The late, or postexanthematous tracheobronchitis is a moot subject. Accompanied, as it is, by very pronounced general disturbances of the health it gives one the impression of tuberculization with discrete apical lesions and frequent small hemoptyses. It is maintained by some very competent writers that these late tracheobronchites merely represent the awakening of an old tuberculous process until then latent, or a bacillary reinfection favored by the specific infection. In practice, it may be said that in nearly all cases tuberculosis will first of all be suspected, simply because syphilis is unsuspected. Clearly the problem is not readily to be solved, but I shall envisage the ensemble of the subject of the association of syphilis and tuberculosis later.

Pleurisy is met with in secondary syphilis, and no lesser men than Chantemesse and Widal, not to mention others, believe that the process is a specific one because of the latent character of the fluid collection, its usual bilateral involvement and the absence of the tubercle bacillus proved by guinea pig inoculation. Other equally competent observers maintain that these data are uncertain, and that usually the process is a latent tuberculosis lighted up by the specific infection, the secondary phase being septicemic probably is anergising, and hence predisposes to tuberculous reactivation. This supposition has been clinically demonstrated by Bezancon and Gastinel.

The tertiary pulmonary lesions are more embarrassing in diagnosis and give rise to frequent mistakes. According to Carrera's statistics, published in 1920, tertiary syphilitic lesions were found in 8 per cent of autopsies on luetic subjects. Besides lesions attributable to acquired syphilis, the part played by late hereditary syphilis may, perhaps, be important, although this point is impossible to determine, as yet.

Acute types of tertiary pulmonary syphilis are exceptional, and the gangrenous form is due—according to Sergent—to superadded infection. The bronchopneumonic form is uncommon, simulates acute tuberculosis and is difficult to diagnose. In most cases tuberculosis is in reality at the bottom of the process.

The chronic types are the most polymorphous, two syndromes having been described: (1) The pseudotuberculous syndrome with a rapid evolution ending in death; or assuming the florid type with an apyretic evolution and good general health, contrasting with the intensity of the pulmonary lesions; (2) The syndrome of pulmonary fibrosis, in which should be comprised a good number of patients who are very frequently cases of unsuspected syphilis. They may present the clinical picture of the asthmatic chronic bronchitis of elderly coughers. Usually the syndrome of bronchial dilatation is present also, and in this respect it is to be recalled that Hutinel has stressed the hereditary syphilitic basis of the majority of cases of bronchial ectasis in childhood. Other observers have advanced the same opinion.

Besides these two principal syndromes, infrequent instances of true diffuse pulmonary syphiloma, simulating cancer or hydatid cyst, have been recorded. Also should be mentioned the association of syphilitic mediastinitis with specific pulmonary or aortic lesions. I am aware of one case in which a man, age 53 years, first developed an acute pulmonary edema followed by nephritis and later by mediastinitis, which led to the diagnosis of unrecognized syphilis and cure by specific medication.

The great frequency of syphilis and tuberculosis renders their association a common occurrence. The older writers, following Hunter's teachings, accepted the general law that a new morbid process arrests the evolution of a preexisting morbid process, hence, according to this law, syphilis and tuberculosis cannot evolute together. Even Laënnec believed that syphilitics were not predisposed to tuberculosis. On the other hand, both Graves and Portal regarded syphilis as a debilitating factor, while, as we all know, Ricord held that this disease facilitated the eclosion of tuberculosis. Fournier differentiated tuberculous lesions, but admitted as possible the association of these lesions with syphilis, because the depressing influence of the latter creates a favorable soil for the development of tuberculosis.

Other observers, especially the French school, hold that the influence of acquired syphilis on tuberculosis varies according to whether or not tuberculosis develops in the full secondary phase or later on. In the former instance it is serious, in the latter case the more remote the onset of the syphilis the less will be the reaction of the syphilis. Sergent and others stress the importance of syphilis as a predisposing factor. Mauriac once said that out of the great number of syphilitics few became tuberculous, unless some other etiologic factor was in play.

The statistics presented by Bezancon and Chevalley at the Fifth National Tuberculosis Congress held at Strasburg in June of this year, show that there were only 6 to 8 per cent positive Wassermanns in children presenting confirmed tuberculous lesions, while in tuberculous adults a positive Wassermann was found in 19 per cent of the cases, according to the statistics offered in 1914 by Letulle, Bergeron and Lépine. It is probable that these percentages are too low, because the Wassermann does not reveal all cases of latent syphilis— far from it—while it is often negative in hereditary syphilis.

In cases of association of inveterate syphilis and tuberculosis, or hereditary tuberculosis, it is still a moot question whether or not the evolution of the tuberculosis is influenced, and whether there exists a special clinical type—a hybrid state of the two morbid processes. Leaving aside all theoretical discussion, and considering the question from a purely clinical standpoint, I think it can be said that scrofulous manifestations, as well as fibrous pulmonary tuberculosis, offer us special clinical types in syphilitic adults, other than the possibility of other coexisting evidences of syphilis, such as aortitis, tabes, a positive Wassermann or the Argyll-Robertson sign. Now, even this coexistence is not common, while in cases of fibrous tuberculosis a negative Wassermann is common; also, from their large autopsy experience, Letulle, Bergeron and Lépine point out that syphilis does not even favor the development of pulmonary sclerosis. However, with our present knowledge, one may assume that, although without absolute proof, lesions of both tuberculosis and syphilis are present, but there is nothing which can lead to the supposition that hybrid lesions exist,—in other words, the famous ''scrofulate of pox'' of Ricord.

The diagnosis of lung syphilis is based upon its differentiation from tuberculosis. The absence of Koch's bacillus from the sputum and a negative result from animal inoculation offer important evidence for the diagnosis of syphilis. But this evidence is not absolute, because if the tubercle bacillus were shown to be present, this fact could not absolutely exclude the presence of syphilis, since the case might be one of association of the two morbid processes. To put syphilis in evidence, *a complete clinical examination is imperative,* including the Wassermann, x-rays and test treatment, which need not be dealt with in this paper.

For a long time gastric syphilis was denied, but at present the reality of this localization can no longer be questioned, and from the surgical viewpoint the subject has become highly important, as Dr. Patry and I have pointed out in our work on the nonmalignant affections of the stomach. ''As to syphilitic gastric lesions, they likewise consist in ulcers and pyloric stenosis, to mention only the more common lesions due to luetic infection. Aaron states that about one out of every seventy-five gastric cases is syphilitic, and that all instances so far observed have occurred during the tertiary phase of the infection.''

''The diagnostic errors to which patients with syphilis of the digestive tract are exposed are legion, the majority of these affections being regarded as local processes or as having a nervous origin. Gastric syphilis in the form of ulcer or cancer is the origin of frequent mistakes. Fournier and Dieulafoy long ago recognized the fact that gastric ulcer was *occasionally* the result of syphilis, and we would add that it is in all probability a frequent etiologic factor. This likewise applies, we believe, to duodenal ulcer . . .''

And farther on we say: ''Two cases of death, recorded respectively by Jacquet and Selenow, following injections of arsenobenzyl, were due to an acute reaction arising in the walls of unrecognized syphilitic gastric ulcers; and Leredde states that he has recently seen a case of duodenal ulcer, that was to be operated on, recover after three injections of novarsenobenzol, so that the operation became unnecessary. We have personally had three cases of gastric ulcer symptomatically cured by specific treatment. Two of these patients gave a history of previous syphilitic infection; the third patient presented a tertiary syphilitic process on the skin at the time he came under observation for the gastric symptoms.[1]''

Leven states in La Clinique, of January, 1922, that he has seen so many gastric ulcers, pyloric stenoses and pseudocancers recover from the exhibition of iodides and Hg, that he systematically advises ''a test treatment'' in every gastropathy that resists ordinary therapeutic measures.

The ulcerating type of gastric syphilis results from the breaking down of a gumma into the cavity of the stomach, and it has only been the rapidly favorable action of a test treatment in a certain number of patients offering symptoms of ulcer that has led to the conclusion that the lesion must be relatively frequent. In my opinion, ulcer is the most frequent form of gastric syphilis.

There are some types which from the onset are hemorrhagic, but without dyspeptic symptoms or pain, and pathologically are due probably to a gummatous arteritis, although I have no proof of this.

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[1] Cumston and Patry: The Surgical Treatment of Nonmalignant Affections of the Stomach, London, Wm. Heinemann, 1923, pp. 310-314.

The small sclerotic syphilitic stomach of Leven and Barret—a true atrophic cirrhosis of the organ—with intense functional disturbances and rapidly developing asthenia presents thick, rigid walls. These diffuse scleroses are sometimes termed "syphilitic linitis."

However, the cicatricial process is more prone to become localized ending in pyloric stenosis, occasionally cardiac stenosis, and more frequently still in midgastric stenosis—the bilocular stomach. That it is an exaggeration to say that all gastric stenoses are syphilitic is unquestionable, but I know of no morbid process but syphilis that is capable of producing multiple bands of adhesions causing several stenoses in the same organ.

Whether or not there is such a process as gastric parasyphilis, I am not prepared to say, but perhaps the tabetic stomach may be the first chapter of the study of gastric parasyphilis.

Regarding diagnosis, I would say that radioscopy is of little help, while the gastric chemism gives very contradictory results. A positive Wassermann shows that the patient is syphilitic, but not necessarily the gastric lesion, and inversely, a negative reaction implies nothing. But in practice, the remarkable and sure results derived from specific treatment will make the diagnosis a quasi certainty.

In 1905, I published a paper in the Arch. f. klin. Chirurgie, entitled "The Surgical Aspects of Hepatic Syphilis," in which I reported several cases where exploratory operation revealed the true condition of affairs; but in what is to follow I shall confine my remarks to the more medical aspects of hepatic syphilis.

The notion that syphilitic lesions may have a febrile evolution is perfectly established, and among those especially prone to cause pyrexia, luetic hepatitis should be placed in the foremost rank. The type of fever, whether intermittent or continued, is uninfluenced by ordinary treatment, but at once subsides under specific treatment. The liver may be generally enlarged or only one lobe may be involved; the surface is smooth or very slightly knobbed; the spleen is only slightly hypertrophied. In those cases with which I am familiar there was no ascites nor symptoms of portal hypertension with, occasionally, a slight subicteric tint.

It is important to recall the extremely rapid results obtained from specific treatment. The temperature drops, appetite returns, the patient puts on weight and the liver becomes normal in size.

Not to appreciate this process has resulted in several diagnostic mistakes; the case may be mistaken for tuberculosis, paludism or ameba infection, and when a negative Wassermann is obtained the unsophisticated practitioners may eliminate the diagnosis of syphilis altogether. Hereditary syphilis is susceptible of presenting similar symptoms, whose interpretation is quite as difficult.

I would also stress the fact that patients with hepatic cirrhosis and ascites are often syphilitics, and when clinical observations and serology have resulted in negative findings a test treatment will often confirm, or even impose, the diagnosis.

The ascites has not invariably a purely mechanical origin, because there may be concomitant luetic lesions of the peritoneum; the small intestine is thickened and retracted to such an extent that it may be shortened as much as one, two or even four meters. Specific treatment will sometimes give really remarkable results. Hence, when in the presence of a case of hepatitis, atrophic or hypertrophic cirrhosis, one must never overlook the fact that although the patient presents the usual clinical picture of these banal morbid processes, the affection may be syphilitic, because there is no pathognomonic distinction, although Letulle and Bergeron found that nearly 50 per cent of the syphilitic cases gave a positive Wassermann. Yet I fancy that in most instances it will be the result of specific treatment and that will settle the diagnosis.

The action of syphilis on the kidney is much more frequent than is generally suspected, because, besides the serious form of albuminuric nephritides, it is likely that late sclerous lesions often commenced during the early months or years of the infection. Renal fragility is unquestionable in syphilitics and should be constantly looked for. It is quite true that the action of drugs on the kidneys is undeniable, and in large doses Hg, arsenic and bismuth unquestionably may have a deleterious effect, but such cases are rather the exception and should not interfere with the specific treatment of renal syphilis.

There are several types of kidney syphilis. In the first place there is the acute and subacute secondary syphilitic nephritis. When it develops in the full bloom of the secondary phase with its concomitant accidents, the diagnosis is generally easy. The urine contains large amounts of albumin and edema is marked.

Chronic nonatrophic nephritis may sometimes develop at once, or it may follow upon an acute nephritis. The diagnosis is easier in the latter circumstance, and more delicate in the former, all the more so because it rarely develops before the second year of the infection and sometimes much later. Its existence may be entirely independent of any other specific manifestations.

The chronic atrophic nephritis that so frequently occurs in syphilis, apparently the result of specific arteritis, offers no clinical characteristic distinguishing it from asyphilitic types, and, in my opinion, most cases having an unknown etiology should be attributed to the trepanema.

The clinical diagnosis of gummatous renal syphilis has never been made during life, as far as I am aware, but I know of its having been mistaken for tuberculosis or malignant disease of the kidney when the gummata have broken down and discharged their débris into the renal pelvis.

Renal amylosis is common in late syphilis of the kidney. It accompanies the sclerogummatous process, although it may be encountered in certain cases of chronic nephritis. It is, moreover, usually associated with lesions in the liver.

Hereditary renal syphilis is never met with clinically, because the infants do not live. The treponema will be found in the kidney as in the other viscera.

Early hereditary syphilis may first show itself by acute nephritis which is rarely diagnosed as syphilitic, unless the infant develops a concomitant specific exanthema.

In late hereditary syphilis the nephritis rarely assumes the clinical aspects ordinarily met with at about the age of ten to twelve years, or more; a transitory or chronic albuminuria occurs with an opaline polyuria. Edema is uncommon; a negative Wassermann must in no circumstance eliminate the diagnosis of hereditary syphilis. Hutinel, whose vast experience is entitled to respect, believes that many instances of orthostatic or familial albuminurias with otherwise good health, are due to syphilitic lesions of the renal parenchyma. In all such cases specific treatment will give remarkable results, and when the Wassermann is negative will settle the diagnosis.

THE WASSERMANN REACTION IN DIABETES

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THERE is a general impression that diabetes occasionally will cause a false positive Wassermann reaction, and that this reaction may not be so significant as in other conditions. Coupled with this is the belief of some, that diabetes is a disease in which the incidence of syphilis is high. However, apparently more has been said than written concerning this false positive tendency in diabetic patients. Literature on this point is scanty, and much of it quite fragmentary. Thus, in 1912, Richards reported that in four of six cases of diabetes with acidosis there was a persistently positive Wassermann reaction, unaffected by treatment for syphilis, and that he knew of only one other such report in the literature. We found only one other preceding report in the literature, that made by Weil and Braun in 1908, of four cases of diabetes in which there were apparently false positive Wassermann reactions, but the high percentage of nonspecific reactions in conditions such as typhus, pneumonia, tuberculosis and cancer makes one strongly suspect deficient technic.

In 1921, Mason, in a study of 168 cases of diabetes, found two apparently false positive reactions. No details were given with regard to his technic. There was no lipemia in either case. Smith also reported one false positive reaction in a case of diabetic coma in a boy, thirteen years of age.

Williams[16] noted sixteen positive Wassermann reactions in 337 cases of diabetes. These were noted especially in severe types of the disease. He said, "As the nutrition improved by proper dietetic measures, there was a coincidental improvement in the Wassermann test." In seven cases under observation it became negative. All sixteen patients had increased lipoid content in the blood. Cholesterol determinations were made on the blood plasmas of eighty-nine patients with negative Wassermann reactions, and thirty-seven of these showed an increase. Williams' determinations were made in two different laboratories which he said were using approximately the same technic, but in a later paper he[17] made this correction: "A review of the data shows that the tests with the unusual variations were made in the Hahnemann Hospital while those performed in the State Laboratory were fairly uniform, consistent and essentially negative." He also stated that the samples of blood from the most seriously ill patients were usually sent to the hospital laboratory, but in view of the great discrepancies, a slight difference in technic with a resulting greater tendency toward false positives cannot, as a whole, be ruled out.

Because of its use in reenforcing antigens in order to make them more sensitive, Williams[16] and others have called attention to a high blood cholesterol as being the possible offending agent. On the other hand, McFarland has shown that the positive Wassermann reaction of the blood does not depend on high cholesterol value. The lecithin content of the blood has not been considered to any extent in this connection, although antigens that are used for various modifications of the Wassermann technic contain lecithin. In fact, antigens have been proposed and used, starting with pure lecithin and cholesterol as the basic substances. It is not far-fetched to argue that changes in the amount of this lipoid in the blood might influence complement-fixation.

Several writers have called attention to the large number of anticomplementary serums in patients with diabetes, especially when "milky," which makes a good reading impossible. Rockwood and Beeler, however, have called attention to the fact that some of these serums, at least, are not really anticomplementary, but that the existing hemolysis is simply obscured by the fat emulsion, since dilution with sodium chloride solution will make the result readable.

Van Saun, in reporting on serums from seventy-three diabetic patients, did not find a false positive tendency. Fifty-one were negative, one was positive, two were doubtful, and nineteen anticomplementary and lipemic. Walker and Haller, in a study of eighty-nine patients with diabetes, found that seven had positive Wassermann reactions, but said, "The majority of these cases gave a history of syphilitic infection."

Rockwood and Beeler have studied the native complement content in the serums of forty-eight patients with diabetes, selected to represent the extremes of metabolic upset, without finding any significant variation.

SEROLOGIC STUDY OF CASES OF DIABETES

At the suggestion of Dr. Wilder, we studied a group of diabetic patients with reference to the existence of false positive Wassermann reactions. For nine months, beginning in January, 1922, a routine Wassermann test was made on every diabetic patient admitted to the hospital for treatment. During the first six months of the use of insulin, the test was made freely, but not routinely. The routine test was again adopted in April, 1923, and continued for five months. But, unfortunately, during the winter period, many patients with severe acidosis were overlooked, since they came in as emergencies, and the Wassermann test either was not made at all, or else after the acidosis had disappeared. Therefore, our list of cases of severe acidosis (Table I), in which the severity of the acidosis and the Wassermann reaction can be compared, is not large.

The Wassermann reaction, as reported in this series, was made by two methods. During 1922 we used the method that had been employed at the Mayo Clinic for eleven years. In this technic is used an antihuman hemolytic system, modified from the well-known Noguchi method, and essentially like that used in the United States Army, and in the Navy Laboratories. The advantages of this system need not be discussed here. Human cells were sensitized with amboceptor overnight in the ice-box. Our amboceptor was made by immunizing dogs with human erythrocytes, as previously described by one of us. Guinea pig complement was used in double unit quantities, determined by titrating 40 per cent dilutions with sensitized cells. The total quantity of reagents was made to a total of 1 c.c. in each tube with 0.85 per cent sodium chloride solution, and complement-fixation was produced by incubation for one hour. Hemolysis occurred quickly after the addition of sensitized cells. The reactions were reported at once, the physician receiving his information the same day that the patient was bled. This system was not sensitive. A total inhibitition of hemolysis was usually diagnostic of syphilis, that is, the tendency toward false positives was small. In fact, because of the tendency toward negative reactions in the presence of latent and treated cases of syphilis, it was decided, after considerable investigation, to change to the more sensitive, well known Kolmer modification. This method was adopted for routine use January 1, 1923; it is far more sensitive, and in the main does not tend to yield false positives. It should be noted, however, that the few instances in which we concluded that there was a false positive reaction, occurred with the Kolmer technic, none with our former nonsensitive method.

DISCUSSION

Serologic examinations were made in a series of 501 diabetic patients seen at the Mayo Clinic in eighteen months. The Noguchi modification technic was employed in 201 of these, and the Kolmer modification in 300 patients seen during 1923. Among these there were eight patients (1.6 per cent) with coincidental syphilis and diabetes. Three of these had negative Wassermann reactions, two by the Noguchi method and one by the Kolmer modification; diagnoses were made by the history or other findings. There were five patients with syphilis whose serology was positive as determined by the Kolmer technic.

The incidence and relationship of diabetes and syphilis in the same patient have been a matter of some discussion. Rosenbloom has given a complete review of the literature on the subject. The incidence in the reports collected by him seems to average less than 6 per cent. In fact, the only work which tends to show a closer relationship is that of Warthin and Wilson, who studied the necropsy findings in six cases of diabetes and found that all showed the histologic changes of syphilis. In four cases spirochetes were demonstrated in the myocardium, and in one case in the pancreas. A study of the pancreas in forty-one cases of latent syphilis showed considerable change in all, but this study has not been confirmed. On the other hand, Simmonds, in 300 necropsies in cases of diabetes, found only twenty cases of syphilis, in seventeen of which there were changes in the pancreas that were not syphilitic. In the other three, the pancreatic changes were such that they might have been ascribed to syphilis. Lemann, also, in a statistical study of 220,000 patients admitted to the Charity Hospital, New Orleans, found that 40 per cent were negroes, who represented 50 per cent of the syphilitic, but only 30 per cent of the diabetic cases.

Williams[16] has criticized Warthin and Wilson's work from the clinical standpoint. No Wassermann reactions were reported in any of the six cases. Of the group of forty-one cases of so-called latent syphilis, no Wassermann reactions were reported in seventeen; they were negative in fifteen, and positive in only nine, while in twenty-five, syphilis was denied or not suspected clinically. In his own series of 126 diabetic patients, Williams[16] was unable to find, by careful examination, any evidence of syphilis.

Of course, valid cases of true gummatous pancreatitis with diabetes are occasionally incorporated in the literature with necropsy reports. Other cases reported as syphilitic pancreatitis on clinical grounds, that is, on the response of diabetes to antisyphilitic treatment, must be regarded with suspicion, since the associated dietary control and the normal fluctuating course of treated diabetes often make a very deceptive improvement in the sugar tolerance. This clinical association of syphilis with diabetes is quite characteristic of a number of recent French writers who diagnose syphilitic pancreatitis on what appear to us to be quite insufficient grounds.

Cases 1, 2 and 3 are possible latent syphilis or doubtful false positive reactions, two tested by the Kolmer method alone, one by both methods.

REPORTS OF CASES

CASE 1 (A408720).—A man, aged thirty-four years, first came to the Clinic in 1922, for treatment of diabetes which had begun in 1919. His only other complaint was of slight paresthesias in the legs. He had had gonorrhea fifteen years before, but there was no history of syphilitic infection, and there were no clinical signs of it on examination. The neurologic examination revealed slight diminution of the deep reflexes and perhaps slight sluggishness of the pupils. There was no acidosis, and the urine was sugar free by October 28, when the routine blood Wassermann test by the Noguchi technic was faintly positive. December 2 it was repeated by the Kolmer method and found to be negative, while another sample was positive by the Kolmer method December 8 and again December 10. The spinal fluid December 16 showed negative Wassermann and Nonne reactions and only one cell.

The patient returned in April, 1923, for further examination. Again there was a little sugar in the urine, but no acidosis. He had had one course of treatment in the meantime. His blood Wassermann reaction (Kolmer method) on April 27 was positive, 21. In this case, the blood Wassermann reaction was positive at times by both modifications of the test.

Case 2 (A419423).—A man, aged twenty-seven years, entered the hospital in March, 1923, with a history of diabetes of three years' duration. He had marked acidosis, his carbon dioxide capacity (Van Slyke method) being 27 per cent. Four days later the total blood fat was determined to be 0.76 per cent. He had had gonorrhea twice, several years before, but there were no other symptoms suggesting syphilis. Two Wassermann tests during this period by the Kolmer technic were positive, 44. A third was taken four days after the glycosuria and acidosis had been cleared up by insulin, and it was still positive, 44. A spinal fluid examination was negative.

Case 3 (A418090).—A man, aged forty-seven years, came to the hospital with very mild diabetes of four years' duration, and no history of syphilis. He came mainly because of his cardiac condition of mitral stenosis with marked cardiac hypertrophy, auricular fibrillation and decompensation. He complained of sharp vertical headaches at times. His routine Wassermann reaction (Kolmer method) was weakly positive, 40. Because of his serious cardiac condition he was sent home without further investigation, which possibly might have revealed latent cerebrospinal or even cardiovascular syphilis.

There were two cases in which the positive reactions by the Kolmer method could not be explained on the grounds of syphilis. It should be noted in the histories that in neither case could the reaction be ascribed to diabetes, as the first was complicated by carcinoma of the liver, jaundice, infection, and lecithinemia, and the second was renal glycosuria.

Case 4 (A435018).—A man, aged fifty-five years, came to the Clinic because of carcinoma of the liver. He complained also of a little weakness in his legs, but neurologic examination was essentially negative. The diabetes was negligible, being readily controlled by a qualitative restriction of carbohydrate. He also had intermittent attacks of slight jaundice, and while in the hospital developed thrombophlebitis of one leg. His routine Wassermann reaction (Kolmer) during an attack of jaundice, was found to be positive, 34. Two other tests made three and six days later, when there was little or no jaundice, were reported negative. Because of his serious condition, no study of the spinal fluid was made and the patient was sent home.

A study of the lipoids of the blood was made by Dr. Georgine Luden at the time the blood was drawn for the second Wassermann test. The cholesterol by the Bloor I method was 136 mg., by the Bloor II method, 177mg., the difference being 41 mg. The normal Bloor I readings are from 70 mg. to 100 mg., but the normal is higher, from 100 mg. to 140 mg., in cases in which there is slight inflammation, such as thrombophlebitis, as in this case. The difference between the Bloor I and II methods is normally from 17 mg. to 34 mg., but 41 mg. is not excessive. The blood lecithin was 615 mg., more than twice the normal of from 290 to 320 mg. The total phosphorus was 119 mg. (normal 76 to 114 mg.), the blood sugar, 110 mg.

We do not believe that the nonspecificity of the one test can be ascribed to the diabetes since it was so mild. On the other hand, Bittorf has reported false positive Wassermann reactions in diseases such as carcinoma of the liver in which there is destruction of an organ rich in lipoids, and Walker and others have described similar reactions in patients with jaundice. The high lecithin in the blood may have been a factor.

Case 5 (A423513).—A girl, aged eight years, came to the Clinic on account of glycosuria. There was nothing in the personal history or examination to suggest syphilis. The only suspicious factor in the family history was that the father had multiple sclerosis, but on several occasions at the Clinic, his examinations, including spinal puncture, had always been negative for syphilis. The routine Wassermann reaction (Kolmer) on admission, was positive, 44. This was repeated twice in the next few days, and was negative both times. The chief point of interest in this case is that it finally proved to be one of renal glycosuria instead of true diabetes; hence the false positive cannot be ascribed to any of the metabolic changes commonly associated with diabetes.

THE WASSERMANN REACTION AND ACIDOSIS

Since many of the reported cases of false positive Wassermann reactions occur in acidosis we are summarizing separately the small group of cases in which the test was taken during severe acidosis. As a measure of the acidosis we have used the carbon dioxide capacity, determined by the Van Slyke method. With the exception of one case, (Case 2), there were no positive Wassermann reactions.

Table I

CASE	CARBON DIOXIDE CAPACITY, PER CENT	WASSERMANN REACTION
		Noguchi Technic
A402666	17	Negative
A264193	16	Negative
A402817	26	Negative
		Kolmer Technic
A422160	27	Negative
A425029	24	Negative
A431269	29	Negative
A423413	22	Negative
A414909	22	Negative
A424662	15	Negative
A426909	30	Negative
A435446	8	Negative
A426298	24	Negative
A432867	30	Negative
A424195	17	Negative
A421280	27	Negative

SUMMARY

We made serologic tests for syphilis in 501 cases of diabetes, 201 by the Noguchi method and 300 by the Kolmer technic. There were eight cases of coincidental syphilis and diabetes, three which may have been latent syphilis or false positives, and two of probable false positive reactions. There is, apparently, only a coincidental connection between syphilis and diabetes in our series of cases. Our study leads us to conclude that the Wassermann reaction is rarely falsely positive in diabetes. In our series of cases a false positive tendency is no greater than in other types of cases with the methods employed. The two probable false positive reactions in our cases cannot be ascribed to diabetes. Furthermore, a review of the literature fails to show valid proof that the reports of false positive reactions in diabetes are any more common than the natural tendency in the methods that the various authors have employed.

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OBSERVATIONS ON THE KAHN PRECIPITATION REACTION FOR SYPHILIS

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SEROLOGIC examination for the presence of syphilis has assumed such an important rôle in diagnosis, that any attempt to simplify the technic or correlate results of various tests seems worthy of effort. The earlier interpretation of the Wassermann reaction as a specific antigen-antibody reaction has been strongly questioned, largely due to the fact that alcoholic extracts of nonsyphilitic organs may be used in the test. It is now becoming more generally believed that the phenomenon is based on physicochemical reactions. That a precipitate actually is formed when a mixture of syphilitic serum and antigen is incubated was first demonstrated by Jacobstahl. During the past few years there have been many attempts to devise a test which would eliminate the hemolytic system, by producing a macroscopic precipitation reaction between serum and antigen. The most important of these so far described are known as the Mienicke, Sachs-Georgi, and Kahn reactions. Although various investigators have found a relatively high agreement between the results of Sachs-Georgi and Mienicke tests and the Wassermann reaction, averaging between 80 to 90 per cent, the prolonged forty-eight hour incubation is a decided obstacle to routine use. Also contamination may occur and lead to false interpretation.

The precipitation reaction as described by Kahn[1] seemed to have several advantages. The technic of preparation of the antigen and performance of the test is very simple, the incubation is relatively short, and the precipitate is easily visible to the naked eye. Furthermore, preliminary studies by Kahn[1] as well as by Keim and Wile,[2] Young,[3] Ide and Smith,[4] and Levine,[5] all seemed to indicate a most favorable correlation with the Wassermann reaction.

For a complete description of the procedure and a discussion of the various factors underlying the reaction, reference is made to Kahn's[1] third communication. In brief our method was as follows: The antigen is prepared by extracting dried ground beef heart four times with ether in the ice box. After freeing the heart muscle from ether extractives and again drying, 5 c.c. of absolute alcohol is added per gram of dried material, and extraction for nine days at ice box, and nine hours at room temperature is carried out. The extract is then filtered off and cholesterinized by adding 4 mg. of cholesterin per cubic centimeter of alcohol. The antigen is diluted for the tests in the proportion of 1 c.c. of alcoholic extract to 1.8 c.c. of physiologic salt solution. The tests proper are performed by combining the antigen salt mixture and inactivated sera in the proportion of 1:6 or 0.05 c.c. antigen to 0.3 c.c. serum. The tubes are shaken thoroughly for five minutes and read after eighteen hours in the water-bath at 37.5°.

After varying different factors in the procedure we have come to the conclusion that the following points are of importance, although the explanation in each case is by no means clear. The preliminary elimination of the ether extractives from the heart muscle is an essential step in the preparation of the antigen. The time element of the secondary period of incubation of the alcoholic extract at room temperature, following the period in the ice box, has a definite effect on the sensitiveness of the antigen. The explanation for this phenomenon may rest with the effect on the lipoid content of the extract, as originally suggested by Kahn. Dilution of the antigen should be carried out within a few hours prior to its employment in the tests proper, in order to insure its optimum sensitiveness. The proper proportion of extract to saline varies in different preparations; the smallest amount, which just prevents spontaneous precipitation, should be used. In our work this was found to approximate a proportion of 1:1.8 c.c. as compared to 1:3 c.c., as recommended by Kahn. If the mixture is made rapidly, a relatively smaller amount of saline can be used without causing spontaneous precipitation, thus increasing the sensitiveness of the mixture. Thorough shaking is absolutely essential for success. Although a few reactions take place within a few minutes after combining serum and antigen, the best plan is to read all tests after eighteen hours in the water-bath. The heavy flocculent precipitates are easily visible whether they tend to clump or not. The finer precipitates require slanting of the tube and reflected light; a hand lens facilitates reading of these. All doubtful reactions should be called negative. A positive and negative serum should be used for control, whenever the test is being employed.

The routine Wassermann technic employed is briefly described as follows: Alcoholic and 0.4 per cent cholesterinized beef-heart antigens are used with an antisheep hemolytic system. Preliminary incubation is in the ice box for eighteen hours, employing 2 units of complement. The incubation period following the addition of the hemolytic system is half-hour in the 37° C. water-bath. The unit of complement is obtained by titrating a $\frac{1}{20}$ dilution of pooled guinea pig serum against one unit of amboceptor and one unit of sheep cells (0.5 c.c. of a 5 per cent suspension) for one-half hour at 37° C. Throughout the test one unit of amboceptor is used. (With the four hour ice box and 37° C. water-bath preliminary incubations only $1\frac{1}{2}$ units of complement are added.)

A comparative study of the Wassermann reactions and Kahn test was made on 1000 sera representing 915 patients. Primary emphasis was placed on clinical evaluation of the two reactions rather than on a laboratory study alone. Clinical data were available in every case, since the patients were either attending the outpatient department, or were on one of the house services of the New Haven Hospital. A large proportion of the syphilitic cases were under treatment in the dispensary. The work was further controlled by examination of repeated samples of blood from the same patient, especially where the original result was doubtful. In each case where the serum showed any reaction to either test, the history of the patient was carefully reviewed and another examination made, if necessary, for possible clinical evidences of syphilis.

The following tabulation represents a comparison of the two reactions on the 1000 sera. The results are classified on the basis of the clinical diagnosis and divided into four main groups, according to the agreement between the diagnosis and the results with each of the two tests. The Wassermann reaction is called ++++ where there is complete fixation with both antigens. For the sake of clarity the term weakly + is used to denote partial fixation with one or both antigens. No differentiation is made between strong and weak Kahn reactions; the test is called either positive or nega-

TABLE I

COMPARISON OF THE WASSERMANN REACTION AND KAHN TEST ON 1000 SERA

A.	Agreement of both tests with clinical diagnosis.			
	Sera of nonsyphilitics	Wass. 0 Kahn 0	706	846 = 84.6%
	Sera of treated syphilitics With negative serology	Wass. 0 Kahn 0	12	
	Sera of syphilitics	Wass. ++++ Kahn +	106	
		Wass. weakly + Kahn +	22	
B.	Disagreement in favor of Wassermann reaction			
	Sera of syphilitics	Wass. ++++ Kahn 0	25	80 = 8.0%
		Wass. weakly + Kahn 0	53	
	Sera of nonsyphilitics	Wass. 0 Kahn +	2	
C.	Disagreement in favor of Kahn test			
	Sera of syphilitics	Wass. 0 Kahn +	8	69 = 6.9%
		Wass. ac Kahn +	14	
	Sera of nonsyphilitics	Wass. weakly + Kahn 0	37	
		Wass. ac Kahn 0	10	
D.	Results unsatisfactory with both tests.			
	Sera of syphilitics	Wass. ac Kahn 0	4	5 = .5%
	Sera of nonsyphilitics	Wass. ac Kahn +	1	

tive to avoid confusion. Anticomplementary reactions are signified by Ac.

From the figures in Table I it can be seen that there is an absolute agreement between the two tests in 84.6 per cent of all sera tested (Group A). There is a disagreement in 8.0 per cent in which the comparison favors the Wassermann test (Group B). There is a further disagreement in 6.9 per cent in which the comparison favors the Kahn test. In the remaining 0.5 per cent the results are unsatisfactory with both tests, but the Kahn result is slightly more misleading. Of course it is at once apparent that the advantage of the Wassermann in Group B is a positive advantage as a better diagnostic aid, while the advantage of the Kahn in Group C is a negative one for the most part (47 out of 69). However, in fairness to the Kahn test it should be pointed out that the apparent disadvantage in Group B is largely due to the fact that most of these sera are from patients who have already undergone rather intensive treatment. The use of a very sensitive Wassermann technic brought out a partial fixation, especially with the cholesterinized antigen, whereas the Kahn test tended to be negative.

Table II is merely a condensed classification, using the initial tests on the 915 different patients rather than the total of 1000 sera. It will be seen that the relative percentages are approximately the same in both cases. Group B and C show greater percentage in Table I because these represent, in the main, the patients in whom repeated samples of blood were examined, usually with similar results. Therefore, the disagreement is slightly accentuated when the sera, rather than the patients, are used as a basis for comparison.

TABLE II

COMPARISON OF THE RESULTS OF THE INITIAL TESTS ON 915 PATIENTS

A. Absolute agreement between two tests	820 = 89.6%
B. Disagreement in favor of Wassermann reaction	48 = 5.2%
C. Disagreement in favor of Kahn test	44 = 4.8%
D. Disagreement, unsatisfactory with both tests	3 = .4%

In Table III the known syphilitic patients are classified according to the type of the disease which they presented upon first admission to the clinic. Under the heading "Late Lesions" are grouped all the late manifestations of the disease other than those of the cardiovascular and central nervous systems, which are classified separately. The term latent applies to the group of patients who show no positive clinical signs of the disease, other than the positive Wassermann. If there was nothing characteristic or suggestive of early or late lesions in the history, the diagnosis of syphilis was not made unless both alcoholic and cholesterinized antigens showed repeated ++++ fixation. In the presence of a

Table III

Classification of Syphilitic Cases According to Type of Disease and Relation to Treatment

	UNTREATED				TREATED			
	Total	Both Agree	Favor Wass.	Favor Kahn	Total	Both Agree	Favor Wass.	Favor Kahn
Primary	2	1	1	0	5	5	0	0
Secondary	10	10	0	0	7	5	2	0
Cardiovascular	3	1	1	1	5	4	1	0
C. N. S.	14	9	4	1	20	9	11	0
Late Lesions	14	11	2	1	20	17	2	1
Congenital	5	3	1	1	10	6	3	1
Latent	24	19	5	0	27	11	15	1
TOTAL	72	54	14	4	94	57	34	3
	Agreement = 75 %				Agreement = 60.3%			
	Favor Wass. = 19.4%				Favor Wass. = 36.4%			
	Favor Kahn = 5.6%				Favor Kahn = 3.3%			

characteristic or suspicious history, repeated partial fixation of one or both antigens was considered a justifiable criterion for making a positive diagnosis.

Unfortunately, during the period in which the work was carried out, only two patients with primary lesions came under observation. Dark-field examination showed Treponema pallida in both of these. In one patient both the Wassermann reaction and the Kahn test were negative. The second case is the subject of special attention (G. C., Case I). It will be noted that all ten untreated cases in the secondary stage showed a uniformly positive test. However, when the late lesions are used as a basis for comparison, the contrast markedly favors the Wassermann reaction. This particularly applies to the treated cases, as pointed out previously. Nevertheless, in fairness to the Kahn test, it should be emphasized again that 23 of the 34 treated cases, who are classified in Table III as favoring the Wassermann test, showed only partial fixation with the Wassermann antigens.

In order to demonstrate this point to our own satisfaction, namely, that the Wassermann test stood out to the disadvantage of the Kahn test in this type of case because of the increased sensitiveness arising from the preliminary eighteen hour ice box method employed routinely, a comparison was made with the four hour ice box and

37° C. water-bath methods on 60 selected cases representing 73 different sera. Those cases particularly were chosen in which there had been disagreement between the Wassermann reaction and Kahn test in the first instance.

The results cannot be represented satisfactorily in table form, but are briefly summarized as follows: In those cases with a negative Kahn test and a ++++ Wassermann by the preliminary eighteen hour ice box fixation method, the four hour ice box or the 37° C. water-bath Wassermann method tended to reduce the degree of fixation. Of 9 such patients, 2 gave ++++ fixation with both the other methods; 2 gave no fixation whatever; and 5 gave less fixation, especially with the alcoholic antigen. In those cases with a negative Kahn test and partial fixation by the eighteen hour ice box method, the other methods tended to cause less fixation or disappearance of fixation altogether. Of 11 such patients 3 were negative by the other methods; 5 gave less fixation, especially with the alcoholic antigen; and 3 gave practically the same results. Even in the 27 cases where the Kahn test was positive, 6 patients showed less fixation with the other methods than with the eighteen hour ice box technic.

In this work the preliminary eighteen hour ice box method was used routinely, because it was believed that a highly sensitive Wassermann technic was desirable for the purpose of contrast with the Kahn test. If the preliminary four hour ice box or 37° water-bath methods had been employed routinely, the Kahn test would have compared much more favorably in the relatively large number of sera of treated cases.

The following ten cases in which more than one sample of blood was examined, are reported individually. The Wassermann is reported on a scale of 4 for each antigen in order to compare the degree of fixation with the different methods. For example, the symbol 4-4 means complete fixation with both antigens; the symbol 0-3 means no fixation with the alcoholic, and +++ fixation with the cholesterinized antigen.

Case 1.—G. C. Primary lesion appeared Dec. 10, 1922. Dark-field examination positive December 15, on which date treatment was begun. The specimens as reported below were taken before administration of salvarsan 0.4 gms.

TABLE IV—CASE 1

DATE	WASSERMANN 18 HR. ICE BOX	 4 HR. ICE BOX	 WATER-BATH	KAHN
12-15-22	0 – 4	0 – 0	0 – 4	0
12-22-22	0 – 4	–	0 – 4	+
12-27-22	0 – 3	0 – 2	3 – 4	+
1- 2-23	0 – 0	–	–	+
1- 5-23	0 – 1	0 – 1	0 – 2	+
1-12-23	0 – 0	–	–	+
1-27-23	0 – 1	–	–	0
2- 6-23	0 – 1	–	–	0

It will be noted that a positive Kahn test appeared on the second specimen after treatment had been begun, whereas there was already fixation with the cholesterinized antigen on the first sample. Also, it is interesting that the specimens of January 2 and 12 gave a negative Wassermann and positive Kahn test.

CASE 2.—L. DeC. A case of aortitis with signs of slight aortic regurgitation, whose chief symptoms are substernal pain and pain in the left shoulder of three years' duration. He had previously received intravenous treatment in 1919, at the conclusion of which he had been told he had a negative Wassermann.

TABLE V—CASE 2

DATE	WASSERMANN 18 HR. ICE BOX	 4 HR. ICE BOX	 WATER-BATH	KAHN
12- 7-22	0 – 1	–	–	0
12-27-22	0 – 4	0 – 4	0 – 4	0
12-29-22	0 – 0	–	–	0
1- 2-23	0 – 2	0 – 4	0 – 3	0
1- 5-23	0 – 4	0 – 4	0 – 2	0
1-16-23	0 – 2	–	–	0
1-23-23	0 – 3	–	–	0

This case represents one of the cases undergoing treatment in which the Wassermann antigens by all three methods show partial fixation, but the Kahn test is consistently negative.

CASE 3.—G. J. A case with classical signs of syphilitic aortitis and aortic regurgitation, who entered the hospital with cardiac failure.

TABLE VI—CASE 3

DATE	WASSERMANN 18 HR. ICE BOX	KAHN
1-12-23	0 – 0	+
12-29-22	0 – 0	0

This represents one of the three cases in which the Kahn test was of more value than the Wassermann as a laboratory aid in the diagnosis of syphilis.

CASE 4.—H. S. A case of early tabes dorsalis with characteristic pupillary and reflex changes and positive serology in the spinal fluid, whose predominant symptoms were gastric in nature.

TABLE VII—CASE 4

DATE	WASSERMANN 18 HR. ICE BOX	 4 HR. ICE BOX	 WATER-BATH	KAHN
11-27-22	2 – 4	–	–	0
12-12-22	0 – 2	0 – 0	0 – 0	0
12-19-22	0 – 0	–	–	0
12-27-22	0 – 4	0 – 4	0 – 2	0
1- 5-23	0 – 4	0 – 4	0 – 1	0

CASE 5.—T. G. A case of asymptomatic neurosyphilis with slight pupillary and reflex changes. The results on the two samples of blood obtained are as follows:—

TABLE VIII—CASE 5

DATE	WASSERMANN 18 HR. ICE BOX	KAHN
1-27-23	2 – 3	0
1-12-23	0 – 0	+

This represents another case in which the Kahn test proved of more value as a laboratory aid in the diagnosis of syphilis on the initial examination of the patient's serum. The result was reversed on the second examination.

CASE 6.—F. F. A patient who gave a history of a primary lesion, but who showed no clinical evidences of the disease on examination. The diagnosis of latent syphilis was made.

TABLE IX—CASE 6

DATE	WASSERMANN 18 HR. ICE BOX	 4 HR. ICE BOX	 WATER-BATH	KAHN
12-15-22	4 – 4	3 – 4	0 – 4	+
12-22-22	3 – 4	–	0 – 4	+
12-27-22	0 – 3	0 – 3	0 – 0	0
1- 5-23	4 – 4	–	–	+
1-16-23	1 – 3	–	–	0

This case illustrates very well the tendency for the water-bath Wassermann to show less fixation, especially with the alcoholic antigen. The Kahn agrees with the water-bath method on 12-27-22, whereas the other two methods show partial fixation with the cholesterinized antigen.

CASE 7.—G. J. A case of typhoid fever with no clinical evidences of syphilis, either in the history or physical examination. The first two specimens were obtained during the febrile stage of the disease.

TABLE X—CASE 7

DATE	WASSERMANN 18 HR. ICE BOX	KAHN
12- 7-22	4 – 0	0
12-12-22	3 – 0	0
12-15-22	0 – 0	0

There is less tendency for the Kahn test to give a false positive during the course of an infectious disease than for the Wassermann. This was also found to be true in three cases of pneumonia, two of rheumatic fever, and one each of active tuberculosis, measles, and septicemia. Six cases of pregnancy and two cases of diabetes also gave partial fixation with the Wassermann antigens, and negative Kahn tests, all of whom showed no clinical evidences of syphilis.

CASE 8.—W. E. A child who entered the hospital in the terminal stage of sepsis. Ante and postmortem blood cultures showed Streptococcus hemolyticus. The two samples below were taken at the same time as the blood for culture. Autopsy showed bronchopneumonia, empyema and pericarditis.

TABLE XI—CASE 8

DATE	WASSERMANN		KAHN
	18 HR. ICE BOX	WATER-BATH	
1-4-23	0 – 0	0 – 3	+
1-8-23	0 – 0	–	+

This represents one of the three cases which gave a false positive Kahn test, all explained on the basis of sepsis. One of the three also had an anticomplementary Wassermann. It is interesting to note that the water-bath technic on the antemortem specimen gave partial fixation with the cholesterinized antigen.

CASE 9.—E. M. A congenital syphilitic with interstitial keratitis and Hutchinson's teeth.

TABLE XII—CASE 9

DATE	WASSERMANN 18 HR. ICE BOX	KAHN
1-27-23	Ac.	+
2- 2-23	Ac.	+
2- 6-23	Ac.	+

In this case there was no question in regard to the clinical diagnosis. However, it illustrates that in the presence of a consistently anticomplementary Wassermann, the Kahn test may be of particular value as a diagnostic aid where the clinical diagnosis is uncertain. There were four patients in this series who had consistently anticomplementary Wassermann and positive Kahn tests, all definitely syphilitic.

CASE 10.—Baby L. The mother is syphilitic with both a positive Wassermann and Kahn test. The first specimen is from the cord at birth. The last specimen was taken following two months of mercurial treatment. To date the child has shown no clinical evidences of early congenital syphilis.

TABLE XIII—CASE 10

DATE	WASSERMANN 18 HR. ICE BOX	KAHN
11-27-22	4 – 4	0
12- 2-22	4 – 4	0
12-19-22	3 – 4	0
1-30-23	0 – 4	0

This is an interesting example which shows that the Wassermann was consistently more sensitive than the Kahn test in this particular case of latent congenital syphilis.

So far our attempts to apply the Kahn test to the spinal fluid have been unsuccessful. However, no thorough study of the problem has been made.

SUMMARY

1. In the few cases of primary lesions which were available for study, there was no evidence to show that the Kahn test became positive before the Wassermann reaction.
2. All cases of syphilis in the secondary stage showed a uniformly positive Kahn test.
3. The discrepancy between the two tests particularly manifested itself in those cases which had undergone intensive treatment. The cholesterinized Wassermann antigen often showed partial or complete fixation in the presence of a negative Kahn test.
4. The sera of only three patients who were definitely nonsyphilitic gave a positive Kahn reaction and these could be accounted for on the basis of sepsis.
5. Three known syphilitic patients, 1 treated and 2 untreated, gave a negative Wassermann and positive Kahn test.

6. The Kahn test did not give a positive precipitation in nonsyphilitic women during pregnancy, in diabetic patients or in cases during the course of infectious disease, all of whom may show partial fixation with the preliminary eighteen hour ice box Wassermann technic, especially with the cholesterinized antigen.

7. A comparison of the eighteen hour ice box, four hour ice box, and 37.5° C. water-bath method on 60 selected cases, representing 73 different tests, reveals that the Kahn reaction approaches the 37.5° water-bath technic in degree of sensitiveness much more closely than it does the more delicate ice box fixation method. Cases which gave partial fixation with ice box methods and negative Kahn tests, usually gave even less or no fixation with the water-bath method.

CONCLUSIONS

1. The Kahn precipitation test is not as valuable a laboratory aid in the diagnosis of syphilis as the Wassermann reaction.

2. The Kahn test seems to be of special value in the following types of cases.

A. Cases in which there is partial fixation with the Wassermann antigens and the clinical diagnosis is uncertain. A positive Kahn test is of confirmatory value.

B. Cases in which the Wassermann reaction is consistently anticomplementary.

C. Emergency type of cases—early lesions or obscure involvement of the central nervous system—where a Wassermann reaction may not be immediately available.

3. The Kahn test has decided merit as a laboratory aid in the diagnosis of syphilis. Further intensive study is indicated in an attempt to increase its sensitiveness, and produce a precipitation reaction which will eliminate the hemolytic system in the serologic diagnosis of syphilis.

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THE FUNDAMENTAL PRINCIPLES OF THE WASSERMANN REACTION

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REGARDLESS of the question of nonspecificity of the Wassermann reaction, it has become generally recognized that it is, nevertheless, fundamentally based upon the principles governing complement fixation through the antigen-antibody reaction. It is also a fact that a better understanding of the test itself is largely depended upon a better understanding of, or additional knowledge regarding these principles.

Erlich's side chain theory of receptors has practically stood unchallenged ever since the work of Bordet and Gengou of applying it to the differentiation of bacteria.[1] It is also probable that if it were possible to remove the so-called receptors of the third order from the blood, in cases of various infectious diseases, and enter them into a neutral medium, such as normal salt, complement fixation could be made an infallible test in all instances where the specific organism is known. However, in the practical application of the test, the fact remains that we are not dealing with these receptors alone, in the medium of the patient's serum, but with many other elements, of allied nature, the true influence of which our knowledge is somewhat lacking.

The writer became very much impressed with this fact early in his Wassermann work, and consequently, outlined a course of original research directed toward determining whether or not any rôle was exercised by the patient's serum, in the Wassermann reaction, other than that of furnishing the specific antibody. Furthermore, in case some definite influence is revealed, toward determining what the elements are upon which such influence is depended. For this work a large series of syphilitic serums of all classes were selected and the results of all experiments carefully tabulated.

Experiment No. 1. This experiment was conducted with serums of the positive plus-minus and one-plus positive class and was directed toward determining the effect of gradually increasing amounts of the patient's serum with the units of antigen, complement, amboceptor and erythrocytes remaining constant. The reasoning was that if there is nothing in the patient's serum other than the specific antibody that in any way enters into the antigen-antibody reaction, it should be possible in the case of serums of low antibody titre to accumulate, through gradually increasing amounts, enough of the specific antibody to give a four-plus positive reaction.

Twenty-four tubes were used for each specimen, and the gradually increasing amounts of serum entered into these were from .005 c.c. to .5 c.c. Two units of complement and two units of antigen were entered into each tube and all incubated at 37.6° C. for one hour. After this two units of amboceptor and .1 c.c. of a 10 per cent suspension of washed sheep's erythrocytes were entered into all of the tubes and all again incubated at 37.6° C. for final reading, which was as per Table I. This table represents about the average result of the series run.

Experiment No. 2. This experiment is the same as that of No. 1, excepting that a series of the 2-, 3- and 4-plus classes were used. The results on an average were as represented in Table II.

The point brought out in the foregoing experiments is that with the amount of antigen, complement, amboceptor and erythrocytes remaining constant, in a series of gradually increasing quantities of serum, all of the positive class have two end points at which complement fixation ceases to take place; one in the order of gradually decreasing quantity and the other in the order of gradually increasing quantity, with the proximity of these points somewhat inversely proportionate to the amount of specific antibody present. It is evident that the former is the result of reaching the point of an insufficient amount of antibody, and, the latter, the result of reaching the point of an apparent excess of serum. The following experiment is directed toward determining the result of a proportionate increase of antigen along with the gradually increasing amount of serum. Apparently some antiantigenic influence is exercised by the patient's serum, so that when a certain excess is reached, the antigen-antibody reaction fails to take place.

Experiment No. 3. A serum of the 2-plus positive class was used for this experiment, and entered into six sets of tubes of twenty-four tubes each in gradually increasing quantities, as in the previous ex-

TABLE I

.500 c.c. SERUM	.400 c.c. "	.300 c.c. "	.200 c.c. "	.100 c.c. "	.095 c.c. "	.090 c.c. "	.085 c.c. "	.080 c.c. "	.075 c.c. "	.070 c.c. "	.065 c.c. "	.060 c.c. "	.055 c.c. "	.050 c.c. "	.045 c.c. "	.040 c.c. "	.035 c.c. "	.030 c.c. "	.025 c.c. "	.020 c.c. "	.015 c.c. "	.010 c.c. "	.005 c.c. "
—	—	—	—	—	—	—	—	—	—	1	1	1	1	1	1	1	1	—	—	—	—	—	—
—	—	—	—	—	—	—	—	—	1	1	1	1	1	1	1	1	1	1	—	—	—	—	—
—	—	—	—	—	—	—	—	—	—	—	1	1	1	1	1	1	—	—	—	—	—	—	—
—	—	—	—	—	—	—	—	—	—	—	—	1	1	1	1	—	—	—	—	—	—	—	—
—	—	—	—	—	—	—	—	—	—	—	1	1	1	1	1	—	—	—	—	—	—	—	—
—	—	—	—	—	—	—	—	—	—	—	—	1	1	1	1	1	—	—	—	—	—	—	—

TABLE II

.500 c.c. SERUM	.400 c.c. "	.300 c.c. "	.200 c.c. "	.100 c.c. "	.095 c.c. "	.090 c.c. "	.085 c.c. "	.080 c.c. "	.075 c.c. "	.070 c.c. "	.065 c.c. "	.060 c.c. "	.055 c.c. "	.050 c.c. "	.045 c.c. "	.040 c.c. "	.035 c.c. "	.030 c.c. "	.025 c.c. "	.020 c.c. "	.015 c.c. "	.010 c.c. "	.005 c.c. "
—	—	—	—	—	—	—	—	—	1	1	2	2	2	2	1	1	1	—	—	—	—	—	—
—	—	—	—	—	—	—	—	1	1	2	2	2	2	2	2	2	1	1	—	—	—	—	—
—	—	—	—	—	—	—	1	2	3	3	3	3	3	3	3	3	2	2	1	1	—	—	—
—	—	—	—	—	—	2	3	3	3	3	3	3	3	3	3	3	3	3	3	2	—	—	—
—	2	2	3	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	3	2	—
4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	3	2

periments. The units of complement, amboceptor and the amount of erythrocytes remained the same throughout, but the antigen used was entered into the different rows of tubes in gradually increasing amounts from 2 to 4 units. The final results were as shown in Table III.

In this experiment it is noted that the end point at which complement fixation fails to take place, in the direction of gradually increasing amounts of serum, is extended according to the increase of the amount of antigen used, while in the direction of gradually decreasing amount this end point remains the same, regardless of the antigen increase. The logical conclusion of the experiments so far is that the patient's serum besides furnishing the specific antibody also contains elements that are antiantigenic and prevent the antigen-antibody reaction from taking place when in the combination of

TABLE III

.500 c.c. SERUM	.400 c.c. "	.300 c.c. "	.200 c.c. "	.100 c.c. "	.095 c.c. "	.090 c.c. "	.085 c.c. "	.080 c.c. "	.075 c.c. "	.070 c.c. "	.065 c.c. "	.060 c.c. "	.055 c.c. "	.050 c.c. "	.045 c.c. "	.040 c.c. "	.035 c.c. "	.030 c.c. "	.025 c.c. "	.020 c.c. "	.015 c.c. "	.010 c.c. "	.005 c.c. "	ANTIGEN
—	—	—	—	—	—	—	—	—	2	2	2	2	2	2	2	2	1	—	—	—	—	—	—	2.0 units
—	—	—	—	—	—	—	—	2	2	2	2	2	2	2	2	2	1	—	—	—	—	—	—	2.4 "
—	—	—	—	—	—	—	2	2	2	2	2	2	2	2	2	2	1	—	—	—	—	—	—	2.8 "
—	—	—	—	—	—	2	2	2	2	2	2	2	2	2	2	2	1	—	—	—	—	—	—	3.2 "
—	—	—	—	—	2	2	2	2	2	2	2	2	2	2	2	2	1	—	—	—	—	—	—	3.6 "
—	—	—	—	2	2	2	2	2	2	2	2	2	2	2	2	2	1	—	—	—	—	—	—	4.0 "

serum, antigen and complement these elements are to a certain extent in excess of the amount of antigen present.

THE NEISSER-WECHSBERG PHENOMENON OF COMPLEMENT DEVIATION

Although presenting the same facts in a slightly different manner, it is plain that the phenomenon brought out in the foregoing experiments is the same as the phenomenon observed by earlier serological workers and studied especially by Neisser and Wechsberg[2] in connection with the action of immune serum upon the specific organism. These men attribute the phenomenon to a deviation of complement through the accumulation to an excess of the specific antibody, maintaining that with such an excess the tendency of the complement is to unite with the unbound antibody rather than with the antigen-antibody complex. In case the excess is great enough, only a small amount of the complement will enter into combination with this complex, while the greater amount is taken up by the free antibody. This explanation is logical enough and is sufficient to cover the facts of the simple experiment of bacteriolysis with immune serums. However, when carried further into the greater complexity of complement fixation, it becomes apparent at least that the so-called deviated complement is not attached to the excess antibody, but is in a free state. If it were not in the free state, it could not act so readily again in the second step of the Wassermann reaction, as shown in the writer's experiments. Furthermore, if an excess of specific antibody is responsible for the phenomenon in question, it should appear first in the order of gradually increasing quantities of serum, in the case of the 4-plus positive class and last in the positive plus-minus class. However, as is noted in Tables I and II, the reverse is true. It appears first in the positive plus-minus class and last in the 4-plus positive class. Whatever the elements are whereupon this phenomenon is depended, as already has been mentioned, it is plain that they do not run in direct proportion to the amount of specific antibody present, but inversely proportionate to the antibody titre.

Experiment No. 4. The natural serological elements of cerebrospinal fluid being somewhat of a different nature than that of the blood serum, a similar experiment to that of Nos. 1 and 2 was carried out with the cerebrospinal fluid of a case of paresis with the view of determining any difference the different serological base of cerebrospinal fluid might cause in the results. Fifteen tubes were used for the experiment, into which the cerebrospinal fluid was entered in gradually increasing quantities from .05 c.c. to 5 c.c. After adding the necessary amount of normal salt to make up the total quantity in each tube up to 5 c.c., 2 units of complement and 2 units of antigen were added to all the tubes and the whole incubated 37.6° C. for one hour. Following this 2 units of amboceptor were added and .1 c.c. of a 10 per cent solution sheep's erythrocytes and the whole again incubated at 37.6° C. for final reading, which was as per Table IV.

Experiment No. 5. This experiment is the same as that of No. 4, excepting that the cerebrospinal fluid of a case of tabes was used. The final results were as noted in Table V.

Experiment No. 6. This experiment was on the order of experiment No. 3, excepting that the cerebrospinal fluid of both a case of paresis and tabes were used instead of blood serum. Twenty tubes were used for each set and three sets were made from each specimen. The quantity of cerebrospinal fluid entered in all sets ran from .05 c.c. to 1 c.c. Two units of complement were entered into all tubes, and a sufficient amount of normal salt to make up a total quantity 1 c.c. The antigen, however, was added into the different rows of tubes in gradually increasing quantities from 2 to 4 units. After the usual period of incubation, 2 units of amboceptor and .1 c.c. of sheep's erythrocytes were added to all tubes and the whole again incubated for final reading, which was as shown in Table VI.

The notable point of the foregoing experiments with cerebrospinal fluid is the fact that there is an absence of any feature on the order of the Neisser-Wechsberg phenomenon of complement deviation, such as is the striking phenomenon of the same experiments with blood serum. This fact makes the matter practically conclusive that the earlier interpretation of this feature is not correct, and that, whatever the elements are upon which it is depended, is present only in the blood and that the specific antibody has nothing to do with it.

THE NATURAL AND ACQUIRED AMBOCEPTOR CONTENT OF THE BLOOD

The principle serological point in which the blood serum differs from the cerebrospinal fluid is the usual presence of native complement and large natural and acquired amboceptor content of various kinds. Noguchi,[3] in his studies of the action of amboceptor and complement upon erythrocytes has elaborately demonstrated that the action of complement is enhanced through the addition of an excess of amboceptor. It is also a well recognized fact that an excessive amount of amboceptor may cause the Wassermann reaction upon a specimen of serum to go negative that otherwise would be positive. In consideration of the writer's experiments with syphilitic serums, the question arises as to how much the natural amboceptor content of the blood might be responsible for the phenomenon brought out, and the experiments to follow are directed toward determining this question.

TABLE IV

.1 C.C. FLUID	.2 C.C. FLUID	.3 C.C. FLUID	.4 C.C. FLUID	.5 C.C. FLUID	.6 C.C. FLUID	.7 C.C. FLUID	.8 C.C. FLUID	.9 C.C. FLUID	1.0 C.C. FLUID	2.0 C.C. FLUID	3.0 C.C. FLUID	4.0 C.C. FLUID	5.0 C.C. FLUID	6.0 C.C. FLUID
—	—	4	4	4	4	4	4	4	4	4	4	4	4	4

TABLE V

.1 C.C. FLUID	.2 C.C. FLUID	.3 C.C. FLUID	.4 C.C. FLUID	.5 C.C. FLUID	.6 C.C. FLUID	.7 C.C. FLUID	.8 C.C. FLUID	.9 C.C. FLUID	1.0 C.C. FLUID	2.0 C.C. FLUID	3.0 C.C. FLUID	4.0 C.C. FLUID	5.0 C.C. FLUID	6.0 C.C. FLUID
—	—	—	—	—	4	4	4	4	4	4	4	4	4	4

TABLE VI

.05 c.c. FLUID	.10 c.c. "	.15 c.c. "	.20 c.c. "	.25 c.c. "	.30 c.c. "	.35 c.c. "	.40 c.c. "	.45 c.c. "	.50 c.c. "	.55 c.c. "	.60 c.c. "	.65 c.c. "	.70 c.c. "	.75 c.c. "	.80 c.c. "	.85 c.c. "	.90 c.c. "	.95 c.c. "	1.00 c.c. "	ANTIGEN
—	—	—	—	—	—	4	4	4	4	4	4	4	4	4	4	4	4	4	4	2.0 units
—	—	—	—	—	—	4	4	4	4	4	4	4	4	4	4	4	4	4	4	2.4 "
—	—	—	—	—	—	4	4	4	4	4	4	4	4	4	4	4	4	4	4	2.4 "
—	—	—	—	—	—	—	—	—	—	4	4	4	4	4	4	4	4	4	4	3.2 "
—	—	—	—	—	—	—	—	—	—	4	4	4	4	4	4	4	4	4	4	3.6 "
—	—	—	—	—	—	—	—	—	—	4	4	4	4	4	4	4	4	4	4	4.0 "

Experiment No. 7. This experiment is directed toward determining the effect upon positive serums of an increase of the natural amboceptor content, through the addition of various amounts of clear cut negative ones. Five serums including the 1-, 2-, 3- and 4-plus positive classes were selected and each specimen divided into three equal parts. One of these parts of each specimen was entered into a series of ten tubes in gradually increasing amounts from .005 c.c. to 0.5 c.c. inclusive. The second part of each specimen was mixed with an equal part of negative serums with a titre of natural antisheep's amboceptor of one unit in .0010 c.c. This mixture of the two serums was entered into another series of ten tubes in gradually increasing quantities from .010 c.c. to .10 inclusive, making the actual amount of positive serum entered into each tube equal the amount of corresponding tubes of the first part. The third part was mixed with the same negative serums as above in proportion of one part of the positive serums to four parts of the negative ones. This was entered into a third series of ten tubes in gradually increasing amounts from .025 c.c. to .25 c.c. inclusive, again making the actual amount of the positive serums entered into each tube equal to amount entered into corresponding tubes of the first part. Two units of complement and two units of antigen were now entered into all of the tubes and the whole incubated at 37.6° C. for one hour. After this two units of amboceptor and .1 c.c. of sheep's erythrocytes were entered into all the tubes and the whole again incubated at 37.6° C. for final reading, which was as per Table VII.

Experiment No. 8. It is noted in the foregoing experiment that the 1- and 2-plus positive classes of serums are completely neutralized through the addition of an equal part of negative serums, having a minimum titre of natural antisheep's amboceptor of one unit in .010 c.c., and that the 3- and 4-plus positive ones are likewise neutralized through the addition of four parts of the same negative serums. In the light of what is known about the effect of an excess of specific amboceptors, the logical conclusion is that the neutralizing effect is probably due to the additional natural antisheep's amboceptor that has been entered into the reaction through the negative serums. In order to determine whether or not this is the case, the same experiment was repeated, using negative serums having a very low titre of natural antisheep's amboceptor, with the results as shown in Table VIII.

It is apparent in this experiment that the natural antisheep's amboceptors are to a great measure responsible for the neutralizing effect of the positive ones, as shown in experiment No. 7. However, since

TABLE VII

.050 c.c. SERUM	.045 c.c. "	.040 c.c. "	.035 c.c. "	.030 c.c. "	.025 c.c. "	.020 c.c. "	.015 c.c. "	.010 c.c. "	.005 c.c. "
4	4	4	4	4	4	4	4	4	4
4	4	4	4	4	4	4	4	4	4
3	3	3	3	3	3	3	—	—	—
2	2	2	2	2	—	—	—	—	—
1	1	1	1	—	—	—	—	—	—

Positive control serum

.100 c.c. SERUM	.090 c.c. "	.080 c.c. "	.070 c.c. "	.060 c.c. "	.050 c.c. "	.040 c.c. "	.030 c.c. "	.020 c.c. "	.010 c.c. "
4	4	4	4	4	3	2	—	—	—
4	4	4	4	4	4	3	2	—	—
3	3	3	2	1	—	—	—	—	—
—	—	—	—	—	—	—	—	—	—
—	—	—	—	—	—	—	—	—	—

Positive and negative equal parts

.250 c.c. SERUM	.225 c.c. "	.200 c.c. "	.175 c.c. "	.150 c.c. "	.125 c.c. "	.100 c.c. "	.075 c.c. "	.050 c.c. "	.025 c.c. "
—	—	—	—	—	—	—	—	—	—
—	—	—	—	—	—	—	—	—	—
—	—	—	—	—	—	—	—	—	—
—	—	—	—	—	—	—	—	—	—
—	—	—	—	—	—	—	—	—	—

One part positive and 4 parts negative

TABLE VIII

.050 c.c. SERUM	.045 c.c. "	.040 c.c. "	.035 c.c. "	030 c.c. "	.025 c.c. "	.020 c.c. "	.015 c.c. "	.010 c.c. "	.005 c.c. "
4	4	4	4	4	4	4	4	4	4
4	4	4	4	4	4	4	4	4	4
3	3	3	3	3	3	3	3	—	—
2	2	2	2	—	—	—	—	—	—
1	1	1	—	—	—	—	—	—	—

Positive control serum

.100 c.c. SERUM	.090 c.c. "	.080 c.c. "	.070 c.c. "	.060 c.c. "	.050 c.c. "	.040 c.c. "	.030 c.c. "	.020 c.c. "	.010 c.c. "
4	4	4	4	4	4	4	4	4	4
4	4	4	4	4	4	4	4	4	4
3	3	3	3	3	3	3	—	—	—
2	2	2	—	—	—	—	—	—	—
1	—	—	—	—	—	—	—	—	—

Positive and negative equal parts

.250 c.c. SERUM	.225 c.c. "	.200 c.c. "	.175 c.c. "	.150 c.c. "	.125 c.c. "	.100 c.c. "	.075 c.c. "	.050 c.c. "	.025 c.c. "
4	4	4	4	4	4	4	3	2	—
4	4	4	4	4	4	4	4	3	1
3	3	3	3	—	—	—	—	—	—
2	—	—	—	—	—	—	—	—	—
—	—	—	—	—	—	—	—	—	—

One part positive and 4 parts negative

these amboceptors probably constitute a large part of the total natural amboceptor content commonly present in human serum, it was decided to determine whether or not any other amboceptors developed to the same height of titre in the negative serums would have the same effect. The usual point of specificity was disregarded in the idea because the writer had no knowledge of any direct data bearing upon this particular question.

Experiment No. 9. Since the natural amboceptors, other than the antisheep's are not commonly present in human blood serum to any marked extent, a high bacterial amboceptor content was built up in three individuals through a course of hypodermic injections of bacterial suspensions in the form of vaccines. The blood of these individuals was also practically free from the usual natural antisheep's amboceptor and had a power to neutralize 4-plus positive serums, as per experiment No. 7, to the extent as shown in Table VIII before the course of bacterial injections were begun.

The bacterial suspensions consisted of a mixture of staphylococci, streptococci, pneumococci and micrococcus catarrhalis and containing 500,000,000 organisms per c.c. Injections were given every third day over a period of six weeks, beginning with one minim and ending with 2 c.c. Ten days after the last injection the blood of these individuals was again tested for the presence of natural antisheep's amboceptor, in order to make certain that this was still absent. The titre in this respect was about the same as originally and the same procedure was now carried out as in experiment No. 7 with three positive serums of the 4-plus class and using the serum of these three individuals for the negative ones. The results are recorded in Table IX.

It will be noted that a most striking neutralizing power of positive serums has been developed in the blood of these individuals and that the neutralizing power of negative serums over positive ones is not confined to the natural specific amboceptors present, but to other amboceptors as well.

Experiment No. 10. Having shown that syphilitic serums, even those of the 4-plus positive class, can be entirely neutralized and made to show a negative reaction, through the addition of negative ones containing a high natural or acquired amboceptor content, this experiment is directed toward determining whether or not it is possible to effect the same neutralization of positive serums within the body,

TABLE IX

.050 c.c. SERUM	.045 c.c. “	.040 c.c. “	.035 c.c. “	.030 c.c. “	.025 c.c. “	.020 c.c. “	.015 c.c. “	.010 c.c. “	.005 c.c. “
4	4	4	4	4	4	4	4	4	4
4	4	4	4	4	4	4	4	4	4
4	4	4	4	4	4	4	4	4	4
Positive control serum									

.100 c.c. SERUM	.090 c.c. “	.080 c.c. “	.070 c.c. “	.060 c.c. “	.050 c.c. “	.040 c.c. “	.030 c.c. “	.020 c.c. “	.010 c.c. “
—	—	—	—	—	—	—	—	—	—
—	—	—	—	—	—	—	—	—	—
—	—	—	—	—	—	—	—	—	—
Positive and negative equal parts									

.250 c.c. SERUM	.225 c.c. “	.200 c.c. “	.175 c.c. “	.150 c.c. “	.125 c.c. “	.100 c.c. “	.075 c.c. “	.050 c.c. “	.025 c.c. “
—	—	—	—	—	—	—	—	—	—
—	—	—	—	—	—	—	—	—	—
—	—	—	—	—	—	—	—	—	—
One part positive and 4 parts negative									

through the building up in the patient's blood of a high amboceptor content by injecting into the circulation appropriate antigens.

Three patients, all of whom were known to have syphilis, were secured for this experiment. All had received considerable specific treatment and were clinically well and showed no other evidence of the disease than a four-plus positive Wassermann reaction, which had persisted over a period of more than a year and apparently had become fixed. Sheep's erythrocytes, tuberculin and staphylococcus aureus suspensions were selected for the antigens, owing to their known antigenic properties. As the first procedure, the patients were given 10 c.c. of sterile washed sheep's erythrocytes, hemolyzed with distilled water, into the gluteal muscle. Considerable soreness followed, but this disappeared again in about ten days, after which a Wassermann reaction was again made, which, however, was the same as previously. A second dose of sheep's erythrocytes was now given, in the same manner as before, with less local reaction and soreness following than before. Ten days after this injection a Wassermann reaction was again run on the blood of all the patients, which was now shown to be only 2-plus positive in each case. A titer was now taken of all the patient's serum to determine the quantity of anti-sheep's amboceptor that had been developed. This was shown, in each case, to be about 1 unit in .0005 c.c. Following this eight injections of Staphylococcus aureus suspension of 500,000,000 organisms per c.c. were given to all of the patients, in gradually increasing amounts from one minim to 1 c.c., over a period of about four weeks. Ten days after the last injection a Wassermann reaction was again made with the blood of all patients, with a clear-cut negative finding in each case. Five months later a two-plus positive reaction was obtained in the case of two of the patients, while the third remained negative. The two showing a positive reaction were given a further course of tuberculin injections, over a period of six weeks, beginning with .001 mg. and ending with 1. mg. A Wassermann reaction taken following this, in both cases, was again found to be a clear-cut negative. The feature of obtaining a negative Wassermann reaction in this manner was so striking that there can be no doubt that it was due simply to the building up of a high amboceptor content in the blood of these individuals other than the specific one.

CONCLUSION

In conclusion of this work, it can be said that the more complete chain of underlying principles upon which the Wassermann reaction is based, and, out of which all problems concerning it are evolved, and, upon which these problems, in turn, must be answered, may be set down as follows:

(1) The Wassermann reaction is fundamentally based upon the principles of complement fixation, through the antigen-antibody reaction, according to Erlich's side chain theory of receptors.

(2) Complement fixation, while theoretically a basis for a specific test for all infectious diseases, encounters difficulties in its practical application, through the fact that specific receptors cannot be dealt with alone in the medium of the patient's serum, but in combination with many other elements of allied nature, the influence of which is uncertain.

(3) The patient's serum, besides furnishing the specific antibody in the Wassermann reaction, exercises an antiantigenic influence in the antigen-antibody reaction so that when a certain excess over the amount of antigen used is entered into the antigen, antibody and complement combination, complement fixation fails to take place.

(4) This phenomenon is on the order of the Neisser-Wechsberg phenomenon of complement deviation, but is not due to an excessive amount of specific antibody, but to the action of elements that are present in specific serums in quantity somewhat inversely proportionate to the amount of specific antibody present and are not present in the cerebrospinal fluid.

(5) These elements constitute the natural amboceptor content of the blood and such other acquired amboceptors that may be present besides the specific ones.

(6) In summary, all of the foregoing facts may be brought together in one broad, but single law, which practically offers a logical explanation of all the important problems confronting the serologists concerning the Wassermann reaction at the present time, and paves the way for both a more delicate and more reliable test for syphilis, according to our present technic, and the possibility of a true specific test, based upon the use of Spirocheta pallida antigens.

In order that the antigen-antibody reaction may take place, in the Wassermann reaction, according to Erlich's side chain theory of re-

ceptors, it becomes necessary that the specific antibody content present constitutes at least a certain minimum per cent of the total amboceptor content present. With the necessary amount of specific antibody present, it furthermore becomes necessary that the amount of antigen used constitutes, either in strength or quantity, at least a certain minimum per cent of this antibody.

The writer is much indebted to the works of Noguchi, especially his elaborately illustrated experiment concerning the results in the hemolytic system of different proportions of complement and amboceptor.[4] Through the suggestion of this experiment much time and work was saved at a point when it was difficult to determine just what the next step ought to be.

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CONTROLLED PROSTITUTION IN COBLENZ, GERMANY

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THE subject of controlled prostitution has been discussed so often and in such detail that it is difficult to present anything entirely new. However, a survey of the situation in Coblenz, Germany, should be of sufficient interest to bear telling. This description applies only to conditions in existence during the time of the American occupation.

When the American forces took over this part of the Occupied Territory, they assumed charge of those activities which necessarily concerned them, but continued the German city and kreis officials, and police and courts in charge of those affairs which pertained exclusively to the German inhabitants. The German laws held for the Germans unless they committed some crime against the Army of Occupation, or some member thereof, in which case the military courts or the courts organized by the United States Army took cognizance. We did not interfere with their civil affairs, or with the execution of their laws, or with their local government, or in fact with anything not necessary. Events have shown this was for the best. They continued their method of police control of prostitution, our only action being to make it impossible for the members of the Army of Occupation to enter the restricted district where the controlled prostitutes resided. I only wish to give a short description of the methods and results of German police control of legalized prostitution as I have seen it in Coblenz, and without many comments. In another paper I will try and describe the clandestine prostitution and venereal disease situation with which the military authorities were confronted.

A woman of legal age may become a controlled prostitute by voluntarily registering herself as such with the police. Everyone in Germany is required to have a card of identification giving the name, age, residence, occupation, photograph, etc., which must be produced when required by the police. Hereafter the card of identification for these women becomes the small prostitute's Observation Book, made much after the manner of a passport and giving her occupation as that of a prostitute. It also contains a series of blank pages which are used by the police physician for keeping a record of the semi-weekly examinations.

A woman may also become a controlled prostitute involuntarily. It is necessary that she be over eighteen years of age, and that her habits and actions be such as to warrant her arrest, and that it be proven or she admit that she has received money from more than one man. If under the legal age, she is ordinarily committed to a home for girls, where she is held under confinement for the length of her sentence. Quite often the inexperienced ones will admit after prolonged examination to receiving money, and thus become automatically registered as prostitutes. The older ones, knowing better, will refuse to make such admissions and continue their occupation with such precautions as may be necessary to avoid the police. They are during this time subject to physical examination and, if found diseased, that is considered sufficient evidence. It should be stated that under the paternalistic governmental activities such as exist in Germany, it is, or at least was formerly, rather difficult for a prostitute to continue her ways for long without discovery.

Following registration, prostitutes are compelled to live under police observation in designated places and to present themselves for police observation twice weekly. I do not believe that any of the larger German cities have restricted districts limited entirely to prostitutes and that all prostitutes are compelled to live in these districts. The examination which is conducted by the Police Physician, generally consists of the following:

1. Examination of the skin and mucous membrane of the mouth.
2. Inspection of external genitalia.
3. Compression of the urethra to determine if discharge be present.
4. Insertion of tubular speculum and inspection of cervix.

It is not the custom in Coblenz to make a routine microscopic examination, since the same physician conducts all examinations and an acute condition would be evident upon inspection. If anyone complained of having received infection from one of the controlled prostitutes, an examination would then be made.

The restricted district in Coblenz is located upon a short street about a block in length known as Wasserthurmstrasse. It has only two entrances, one at each end. From the beginning of the occupation, this street was declared and marked "Off Limits" to all members of the Army of Occupation, and a competent guard was kept stationed at each entrance day and night. Consequently the results obtained were nearer that to be expected among the German population under normal conditions. This would not hold absolutely as due to the military occupation; there was a greater number of clandestine prostitutes and a higher rate of venereal disease among them, to which in the nature of things the civilian population was to a certain extent exposed. Coblenz is a city of about 60,000 inhabitants, but for many years has been a military center and, as a result, there has always been a considerable amount of venereal disease and clandestine prostitution.

At the time this paper was written (March, 1923), there were thirty-three controlled prostitutes in Coblenz, of whom thirty-two lived in the restricted district. The thirty-third will be mentioned later. As will be noted later from their ages, they were rather a mature lot of women and in spite of the years engaged, did not have the dissipated appearance which is so characteristic of the American prostitute even after a short period. They had, on the whole, a very healthy appearance and Dr. Fetter, the Police Physician, stated that their general health was quite good.

They are only permitted to live one in a house where they must remain when guests are present. The presence of a third person will, if discovered, subject them all to fine and imprisonment, especially the one in whose house the party takes place. Intoxication or the use of drugs is also a cause for fine and imprisonment. In the Coblenz district three of the women own their own houses, the others are renters. Dr. Fetter stated that they all seemed to be happy and contented. They are allowed, if they wish, to have an authorized woman come in each day and clean up their houses and prepare meals. One of the frugal women who owns her own house, stated that she does all her own work and, from top to bottom of the house, all was in the best of condition. According to the information furnished me, some of the more mature women seem to be equally as popular as some of the younger.

The present police physician, who is an unusually competent and reliable man, has been in charge of this work for four years. He gave me the following information for this four-year period for the controlled prostitutes in Coblenz:

Number of fresh cases of gonorrhea observed	2.
Number of primary and secondary syphilis	0.
Number of men who claim to have been infected by them	0.
Average number under control for this period	34.
Number now present	33.
Number now present giving positive Wassermanns	7.
Number with weak Wassermann reactions	2.
Number with negative Wassermann reactions	24.
Number of cases of acute adnexal involvement observed	0.
Maximum age	48.
Minimum age	26.
Average age	36.5
Maximum years registered as controlled prostitute	18.
Minimum years registered as controlled prostitute	4.
Average years registered as controlled prostitute	13.3

It should be stated that the complement-fixation tests were performed at the City Laboratory and that the work done there is of a reliable character.

The examinations are performed twice weekly in a room prepared for the purpose in the restricted district. The police physician is accompanied by a police official or clerk who remains in the outer room and checks off in a register those who are examined. A police matron assists in preparing the room and solutions and sterilizing the instruments. Following each examination, the police physician makes the necessary notation in the Observation Book of the woman.

I was interested in learning Dr. Fetter's opinion of the situation in Coblenz, as compared with other places in Germany, since he has had excellent opportunity for observation. As with other data, the question was submitted and the answer returned in writing. It will be of interest to give a fairly literal translation of both question and answer: (Q.) "Do you think that conditions in Coblenz are fairly characteristic of those existing throughout Germany, or might it be possible that careful inspections and a rigid enforcement of restrictions have obtained better results here than elsewhere?" (A.) "So far as I know, the control in the remainder of Germany is as strictly applied as here in Coblenz. There is, however, a difference between the larger and smaller cities. In the larger cities the prostitutes are permitted to spread out and are not kept in a restricted area. They must, however, submit to police and medical control. In smaller cities, as Coblenz, a segregated district is employed, that is, the prostitutes are limited to certain streets and houses as dwellings. The latter method of handling prostitution I believe to be the better one, because in this manner a more strict police control and better medical examination is possible. Otherwise the prostitutes can more readily escape or avoid control, and thereby increase the danger of spreading venereal disease. This method or possibility of spreading venereal disease is known as clandestine prostitution. These women follow their immoral business, evading control by means of frequent changes of dwelling, so that there is the greatest danger to health."

Throughout Germany, it is the custom to send all diseased prostitutes to a hospital where they are treated at government expense. In case they have venereal disease, they are held under restraint, and only released when it is thought safe to do so.

Some of the fundamental legal regulations governing the control of prostitution are contained in the paper which the prostitute is compelled to read and sign, and also in her Observation Book. They are as follows:

1. Each change of dwelling, each departure, and each return must be reported to the police within twenty-four hours.
2. She must submit herself to the examination of the Police Physician.
3. Designation of time and place for such examinations.
4. She must follow the instructions of the Police Physician and the supervising officials.
5. In case of venereal, or other contagious disease, or suspected disease, she must go immediately to a hospital or a place of treatment for the sick until recovery ensues, and must obey all rules of the institution.
6. She must procure this Observation Book at her own expense and keep it with her constantly.
7. This Observation Book must be shown to any of her guests who request it.
8. She must purchase an irrigator and use it following each menstrual period, before the examination of the Police Physician.

9. She must follow out scrupulously the prophylactic measures accompanying these rules.

10. She must furnish a copy of her photograph for the Observation Book, and one to the Police.

11. The police officials shall be permitted entrance to her house at any time.

The following is forbidden:

1. To attract or entice men, to appear improperly dressed in the door, window, or on the street. To attract attention by striking on the window or shutter. To leave the doors open, or the windows uncovered, so that one in the street may see into an inner room.

2. To dwell in streets, places or houses not permitted by the police.

3. She shall not shelter other prostitutes, nor male companions, and, during the visits of men, shall allow no other person in the house.

4. She shall not associate with those under age, or dwell in the families of those having children of compulsory school age.

5. She shall not employ cleaning women or other servants without police permission.

6. She shall not leave her house after sunset except for the most urgent reasons.

7. She shall not furnish alcoholic drinks in her dwelling or permit men to drink them there.

8. She shall not be guilty of scandalous behavior in public.

The transgression of these regulations will be punished by up to six weeks' confinement. Similarly also in case of conviction in the National Police Courts, she will be sentenced to a prison or a reform institution up to two years.

The nonobservance of the regulations dealing with health will, according to the provisions of the Prussian law, be punished with a fine or by imprisonment.

The deliberate violation of the regulations prescribed by the authorities concerning the prevention of the spreading of venereal diseases will result in an imprisonment up to two years, or a fine.

The deliberate or negligent transmission of a contagious disease to another is punishable under the law of assault with a fine, or imprisonment up to three years, and under certain conditions with a penitentiary sentence at hard labor.

Finally I am aware that the removal of control follows upon the establishment of a morally pure conduct of life, and the adoption of an honorable and unobjectionable occupation.

Read through, accepted and subscribed to,

In testimony thereof:

Signature ....

Prophylactic measures accompanying:

For keeping the body clean and especially the genitalia, soap and water shall be used at least once daily. At least once weekly, a warm, full bath shall be taken and the body well soaped.

After each intercourse, the vagina shall be washed out with the aid of the vaginal douche and the irrigator. For that purpose water should be used which has dissolved in it a sufficient quantity of potassium permanganate to give a red wine color. Also, pure acetic acid or aluminum acetate solution (2 to 3 teaspoonfuls to a liter of water) may be used.

The greatest cleanliness of the entire body is a good means of protection against venereal disease.

Intercourse should not be held with men in whom it is possible to expel mucus or pus from the urethra by pressure, or upon whose members red spots or ulcers are visible. Sexual intercourse with such men will invariably result in contracting disease.

Where a woman is dependent upon her own exertions for support, as is the average prostitute, it is not easy to get out from under police control, for the reason that positions are not readily secured by those whose identification card is that of a prostitute. Marriage will accomplish the result automatically, but it is obvious that this is a method which would not ordinarily be available. When a woman declares that she wishes to change her method of life, she is permitted to change her dwelling provided she can give reasons which are satisfactory to the police. She is then kept under observation by the police for a period of six months, during which time she is compelled to make the usual reports and submit to the usual examinations. At the end of this period if everything is satisfactory, she is given a new identification card and released from control. Her official or legal record which is kept for all German citizens will, however, bear the information that she has been a controlled prostitute. At the time this paper was written, there was one such in the city of Coblenz who was living with her parents, and was to be soon released from control.

I had the opportunity to make some inquiries concerning conditions in Bonn, Frankfort, and Dresden. These are larger cities and do not have an absolute restricted district as in Coblenz where control can be so readily applied. The results obtained are about what would be expected, or at least I so take it from the general information furnished me, and not in any way unusual as in Coblenz.

ON THE PREVENTION OF SYPHILIS OF THE CENTRAL NERVOUS SYSTEM

By Sahachiro Hata

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IT is more than ten years since salvarsan found its practical application, yet to my regret I have to speak on syphilis of the central nervous system, a calamity which is a cause of suffering to the patient, worry to the family, and a menace to society. If salvarsan has the power to cure syphilis in the early stage, and really does cure it, the number of cases of cerebrospinal syphilis occurring on an average of ten years after infection should be reduced to some degree, by this time, below that of the presalvarsan era. What do the facts show? There are men who say that central nervous syphilis occurs rather more frequently since the introduction of salvarsan, and that its manifestations appear earlier than before. At any rate, it cannot be said that the number has decreased. Is the modern antiluetic treatment so ineffective that it is unable to cure syphilis in the early stage? When we consider syphilis in the other parts of the body, except the central nervous system, we will recognize that the present antiluetic treatment gives far better results than that of the presalvarsan era, and that a large percentage of cures is obtained if an energetic treatment is instituted in the very early stage. The causative organisms of syphilis, however, not only multiply in the primary lesion from the very beginning, but they invade the whole body. In the very early period the organisms invading the blood are destroyed by the natural spirocheticidal power of the blood, but in three or four weeks they become so-called serum fast and multiply in the blood and spread all over the body. This is the beginning of the secondary stage. It is in the lymphatic spaces of the connective tissue where, by choice, they live, multiply and lie in hiding. During the early stage even when the organisms are easily destroyed in the blood they escape there the influence of the spirochetocidal action of the blood which only with difficulty reaches the lymphatic spaces. The lymph which surrounds the cerebrospinal nerves is the place where the defensive action of the blood, or the effect of the antiluetic drug injected into the blood, is the most difficult to reach. It is natural that in the beginning of the second stage when the spirochetae multiply rapidly and spread all over the body that occasionally some of them enter into the cerebrospinal lymph fluid. If once they settle there, they escape the action of the drug in the vigorous antiluetic treatment, which is a little short of absolute sterilization, and establish there seats of infection, from which they have occasional flare-ups or attach themselves deep into the nerves. Thus the fate of the patient concerning the central nervous system is already determined in the secondary stage.

Clinicians have noticed for a long time that general paralysis and tabes occur more frequently in syphilitic patients who had dormant signs and not external symptoms. On the other hand, they occur less frequently in patients who have various external symptoms on the skin, mucous membrane, internal organs or bones. For this reason there are some who claim to have demonstrated the existence of a special neurotropic strain. It has no firm evidence, however, to be accepted generally. It is, however, generally accepted that superinfection with syphilis is very rare. While the disease process is active in the predisposing seats of syphilis, such as the skin or mucous membranes, the spirochetes in the central nervous system remain dormant, but they become active when there are no competing processes in the other parts of the body. If this explanation is accepted, then the fact that the increase in the number of the so-called nervous relapses or metasyphilis, and all such syphilis of the central nervous systems or neighborhood, can be easily understood because since the introduction of salvarsan the syphilis other than that in the nervous system is, by far, more completely cured than before. In order to prevent the grave outcome of syphilitic infection the antiluetic treatment during the second stage should be energetically carried out. The treatment should be pushed to absolute sterilization of the cerebrospinal fluid, and one should not be satisfied with the resolution of the external symptoms or the disappearance of the Wassermann reaction of the blood.

The route of entrance of the spirochetes into the cerebral nervous substance is by the way of the vessel walls and perivascular lymph spaces. Therefore, they spread and multiply in the meninges, especially in the lymph of the leptomeninges. Thus the subarachnoidal lymph space is the most favorable place for the spirochetes to multiply. After they have multiplied in this place they enter into the cerebrospinal substance through the lymph channels into the connective tissue or the capillary blood vessels. In so-called cerebrospinal syphilis the diseased foci are present in the vessel walls or in the connective tissue. The involvement of the nerve substance, as in paralysis or tabes, follows only in the last stages. Therefore the beginning of a syphilitic infection of the central nervous system is a cerebrospinal meningitis. Even after the disease process has advanced to the nerve substance the cerebrospinal meninges and their connective tissues are still more or less affected with the disease. For the prevention of cerebrospinal syphilis great importance should be attached to the so-called early syphilitic meningitis.

The early syphilitic meningitis occurs at the end of the primary stage, and especially in the secondary stage when the spirochetes are actively spreading all over the body. There are wide differences in the severity of the symptoms. In a severe case, there are intense headaches, stiffness of the neck, vomiting, and insomnia or convulsions, but these are rather rare. In most cases, there appear only one or two uncertain symptoms such as headaches, heaviness of the head, slight dizziness, nausea, vomiting, uneasiness of sleep, ringing of the ears, disturbances of the olfactory, trigeminal or facial nerves, weakness of muscle power, a feeling of fatigue, depression of the mind, nervous debility, palpitation of the heart or slight fever. In a very mild case there are no subjective symptoms whatever, and the diagnosis is made only by the test of the spinal fluid. It is ideal to make lumbar punctures in all patients in the secondary stage, but it is hardly practicable. In ordinary practice, by careful examinations in the early stage of syphilis, some of these symptoms aforementioned may be detected, which lead one to suspect the presence of early meningitis. It is not too late then to make an examination of the spinal fluid. With this plan I have examined in recent years about one thousand syphilitic patients, and the spinal fluids were tested in one hundred and twenty cases

TABLE I

RESULTS OF THE TESTS OF BLOOD AND SPINAL FLUID AT THE FIRST CLINICAL EXAMINATION.

CLINICAL DIAGNOSIS		PRIMARY STAGE		SECONDARY STAGE		LATENT SYPH.		TERTIARY STAGE		SPINAL SYPH.		BRAIN SYPH.		TABES		DEMENTIA PARALYTICA		TOTAL	
NO. OF PATIENTS		3		16		30		5		15		21		23		7		120	
BLOOD WASSERMANN		POS. 2	NEG. 1	POS. 15	NEG. 1	POS. 30	NEG. 0	POS. 4	NEG. 1	POS. 15	NEG. 0	POS. 16	NEG. 5	POS. 16	NEG. 7	POS. 7	NEG. 0	POS. 105	NEG. 15
CEREBROSPINAL FLUID (POSITIVE)	GLOBULIN	0	0	7	1	8	0	3	0	12	0	13	5	14	7	7	0	64	13
	CELLS	0	0	4	1	3	0	2	0	11	0	11	4	13	7	7	0	51	12
	WASSERMANN	0	0	4	1	2	0	2	0	10	0	10	3	13	7	7	0	48	11
	CASES*	0	0	7	1	9	0	3	0	12	0	13	5	14	7	7	0	65	13

*The figures in this line denote the number of patients in whom one or more than one of the three tests proved positive.

in which I suspected nervous disturbances at the first examination. The results of the tests are shown in Table I.

The most important cases in the table are those in the secondary stage. Out of the sixteen cases there are eight patients who had changes in the spinal fluids. One of these cases had a negative blood Wassermann, while the spinal fluid gave positive results with all tests.

The blood Wassermann reaction has no decisive meaning in the diagnosis of syphilis of the central nervous system. The patients with brain syphilis or tabes often give negative blood Wassermanns, while the spinal fluids give positive reactions. In a case of tabes, when the blood Wassermann is positive, there is no way to know whether or not this positive reaction is due to other syphilitic lesions, for instance vascular syphilis, which often accompanies tabes. It is a well-known fact among those who have had experience with neurosyphilis that the blood Wassermann may become negative after antiluetic treatments while the changes in the spinal fluid do not disappear. Therefore, it is very important to examine the spinal fluid at the end of treatment of early syphilis so that neurosyphilis in the later stage may be prevented.

Among the tests of the spinal fluids, the number of leucocytes is markedly increased in cerebrospinal meningitis, especially in acute cases. In some cases the cell count reaches as high as eight hundred or one thousand cells in one cubic millimeter. Meningitis always accompanies brain syphilis, therefore the cells are more or less increased. When only the blood vessels are affected the cells are rarely increased, but they are increased in dementia paralytica. The number of leucocytes fluctuates very markedly. It increases rapidly when the meningitis becomes acute, and decreases when it becomes chronic, and it responds easily to treatment. It proves that syphilitic meningitis is easily influenced by treatment. Therefore, the large number of cells alone does not necessarily indicate a bad prognosis. Next most easily influenced by treatment is the Wassermann reaction. The most difficult to clear is the globulin. The number of cells may be decreased by simple intravenous injection of salvarsan, but the Wassermann reaction is weakened only after repeated intravenous injections or by some methods like the Swift-Ellis. Globulin can hardly be cleared by continuing the treatment energetically, even if the others have become negative. The prognosis is good if the Wassermann reaction is weakly positive, even when the cell count is large. On the other hand, when the Wassermann and globulin reactions are strong even if the cell counts are low, it indicates that the disease has penetrated deeply into the nerve substance and the prognosis, as a rule, is bad. At any rate, early syphilitic meningitis is a hopeful case for treatment, because the diseased seats are situated near the meningeal blood vessels easily reached by drugs. Therefore, even simple mercury treatment may be able to reduce the inflammation to a certain extent, and intravenous injections of salvarsan often show wonderful effects. The cases of neurorelapses are in the same category. If the seats of the disease in the cerebrospinal syphilis are limited to the vascular walls they are easily acted upon by the drugs, and with the cure of the diseased foci the nutrition of the territory of the brain supplied by the affected vessel is recovered, and at the same time its lost function is often regained. But the hope of recovery is very slight when the degeneration has taken place in the affected brain substance. The brain substance may have degenerated in paralysis or tabes, but there remain active spirochetes, so that if antiluetic treatment is instituted as early as possible, it may improve the condition to a certain degree. Especially those various local treatments originated by Swift, Ellis and others bring forth improvements to the central nervous syphilis in all the stages more decisively than by intravenous injections, as I have experienced myself, and I feel grateful to the originators. The cure of neurosyphilis in the last stage, however, is, at the most, only symptomatic. Thus, there are not a few cases of practical cures of such a degree that they may be able to engage in daily occupation. But I am sorry to say that entirely negative results in all the tests of the spinal fluid are gained only in very rare cases. In other words, absolute cure is unusual. There is a wide difference when it is compared with the ease of cure of early meningitis or localized syphilis of meningeal vessels.

In short, it is necessary to prevent neurosyphilis before it has occurred, by discovering the invasion of syphilis into the central nervous system in its early stage and destroying it as early as possible. By doing so one will surely be amply rewarded and a menace to society may be removed.

EPOCH-MAKING CONTRIBUTIONS TO THE STUDY OF SYPHILIS

AMBROISE PARÉ

Of the Lues Venerea, and Those Symptomes which Happen by Meanes Thereof—The Nineteenth Booke.

CHAPTER I

A DESCRIPTION OF THE LUES VENEREA

THE French call the Lues Venerea, the Neapolitane disease, the Italians and Germans (as also the English) terme it the French disease, the Latines call it Pudendagra, others name it otherwise. But it makes no great matter how it bee called, if the thing itself bee understood. Therefore the Lues Venerea is a disease gotten or taken by touch, but chiefly that which is in uncleane copulation; and it partakes of an occult quality, commonly taking its originall from ulcers of the privic parts, and then further manifesting its selfe by pustles of the head, and other externall parts; and lastly, infecting the entrailes and inner parts with cruell and nocturnal tormenting paine of the head, shoulders, joynts, and other parts. In processe of time, it causeth knots and hard Tophi, and lastly corrupts and foules the bones, dissolving them, the flesh about them being oft-times not hurt; but it corrupteth and weakeneth the substance of other parts, according to the condition of each of them, the distemper and evill habit of the affected bodies, and the inveteration or continuance of the morbificke cause. For some lose one of their eyes, others both, some lose a great portion of the eyelids, othersome looke very ghastly, and not like themselves, and some become squint-eyed. Some lose their hearing, others have their noses fall flat, the pallat of their mouthes perforated with the losse of the bone Ethmoides, so that instead of free and perfect utterance they faulter and fumble in their speech. Some have their mouthes drawne awry, others their yards cut off, and women a great part of their privities tainted with corruption. There bee some who have the urethra or passage of the yard obstructed by budding caruncles, or inflamed pustles, so that they cannot make water without the helpe of a Catheter, ready to die within a short time, either by the suppression of the urine, or by a Gangrene arising in these parts, unlesse you succour them by the amputation of their yards. Others become lame of their arms, and othersome of their legges, and a third sort grow stiffe by the contraction of all their members, so that they have nothing left them sound but their voice, which serveth for no other purpose but to bewaile their miseries, for which it is scantly sufficient. Wherefore should I trouble you with mention of those, that can scantly draw their breath by reason of an Asthma, or those whose bodies waste with a hectic feaver and slow consumption? It fares farre worse with these, who have all their bodies deformed by a Leprosie arising therehence, and have all their throttles and throates eaten with putride and cancrous ulcers; their hair falling off from their heads, their hands and feet cleft with tetters and scaly chinkes; neither is their case much better, who, having their braines tainted with this disease, have their whole bodies shaken by fits of the falling sickness; who troubled with a filthy and cursed flux of the belly, doe continually cast forth stinking and bloudy filth. Lastly, there are no kinds of diseases, no sorts of symptoms, wherewith this disease is not complicate, never to be taken away, unlesse the virulence of this murrain be wholly taken away, and impugned by its proper Antidote, that is, argentum vivum.

CHAPTER II

OF THE CAUSES OF THE LUES VENEREA

There are two efficient causes of the Lues venerea; the first is, a certaine occult and specificke quality, which cannot be demonstrated; yet it may be referred to God, as by whose command this hath assailed mankind, as a scourge or punishment to restraine the too wanton and lascivious lusts of unpure whoremongers. The other is an impure touch or contagion, and principally that which happens in copulation. Whether the man or woman have their privities troubled with virulent ulcers, or bee molested with a virulent strangury (which disease crafty whores colour by the name of the whites) the malignity catcheth hold of the other; thus a woman taketh this disease by a man casting it into her hot, open and moist wombe; but a man taketh it from a woman, which, for example sake, hath some small while before received the virulent seed of a whore-master polluted with this disease, the mucous sanies whereof remaining in the wrinckles of the womans wombe, may be drawne in by the pores of the standing and open yard, whence succeede maligne ulcers, and a virulent strangury. This virulencie, like a torch or candle set on fire, will by little and little bee propagated and sent by the veines, arteries and nerves to the noble parts; whose malignity a strong liver not enduring, by the strength of the natural expulsive facultie, will fend it into the groines, whereon follow Abscesses, therefore called venereall Bubo's. These, if they returne againe, and cast not forth matter by being opened, they will, by their falling back into the veins and arteries, infect the masse of the bloud by the like tainture, and thence will ensue the Lues venerea. Yet this disease may be got by a more occult manner of touch, as by breathing only. For it is not altogether besides reason and experience, that a woman longtroubled with this disease, may by importunate and often kissing, transfuse malignity into a childe; for the tender and soft substance of a little childe may bee altered, infected, and by little and little corrupted by receiving of filthy and in their whole kinde maligne vapours. For it is knowne, and now vulgarly believed, that mid-wives by receiving the child of a woman infected with this disease, to have got this affect, the malignity being taken and drawne into their bodies through the pores of their hands by the passages of the veines and arteries. Neither doth it spare any condition, sexe, nor age of men; for, not onely whosoever use copulation, but such as onely lye with them, may bee taken by this virulencie; yea verily, if they onely lye in the sheets or coverings which retain his sweat, or the virulencie cast forth by an ulcer. The same danger may assaile those who shall drinke in the same vessell after such as are troubled with this disease. For by the impure touch of their lips, they leave a virulent fanies and spittle upon the edges of the cup, which is no lesse contagious in its kinde than the virulencie of leprous persons, or the fome of madde dogs. Wherefore it is no marvell if children nursed by an infected nurse, draw in the seeds of this disease together with the milk, which is only bloud whitened in the breasts;

or infected sucking children by their hot and ulcerated mouthes, may transfuse this malignity into the body of the nurse, by the rare, loose and porous substance of the dugs which it frequently sucketh.

This following history is very memorable to this purpose. A certaine very good Citizen of this Citie of Paris granted to his wife being a very chaste woman, that conditionally shee should nurse her owne child of which shee was lately delivered, shee should have a nurse in the house to ease her of some part of the labour; by ill hap, the nurse they tooke was troubled with this disease; wherefore shee presently infected the childe, the child the mother, the mother her husband, and hee two of his children who frequently accompanied him at bed and board, being ignorant of that malignity wherewith hee was inwardly tainted. In the meane while the mother when shee observed that her nurse childe came not forward, but cryed almost perpetually, shee asked my counsell to tell her the cause of the disease; which was not hard to bee done, for the whole body thereof was replinished with venereall scabs and pustles, the hired nurses and the mothers nipples were eaten in with virulent ulcers; also the fathers, and the two other childrens bodies, whereof the one was three, the other foure yeares old, were troubled with the like pustles and scabs. I told them that they had all the Lues venerea, which tooke its originall and first offspring by maligne contagion from the hired nurse. I had them in cure, and by Gods helpe healed them all, except the sucking child, which died in the cure. But the hired nurse was soundly lashed in the prison, and should have beene whipped through all the streets of the Citie, but that the magistrate had a care to preserve the credite of the unfortunate family.

CHAPTER III

IN WHAT HUMOUR THE MALIGNITY OF THE LUES-VENEREA RESIDES

Though in the opinion of many the antecedent cause of this disease be the masse of bloud conteining the foure humours, yet I had rather place the matter, and primary, and chief seat thereof in grosse and viscide phlegme infected with the maligne quality of the venereous venome, and from this beginning and foundation, I thinke by a certaine contagious growth it sooner or later infects the other humours, as each of them is disposed or apt to suffer. Of which my opinion there are many arguments, but this chiefely, That by the evacuation of a phlegmaticke humour, whether by the mouth and salivation, or by stoole, urine, or sweate in men of what temper soever, whether cholerick, sanguine or melancholy, the disease is helped or cured. Secondly for that the excesse of paine is more by night than by day, because then the phlegme bearing sway, severs the perioftium from the bone, or else offends it and the rest of the membranous and nervous bodies by the acrimony of its malignity. Thirdly, because the patients are hurt by the use of cold things, but usually finde benefit by hot medicines, whether they bee oyntments, plasters, fumigations, or whatsoever else, inwardly taken, or outwardly applyed. Fourthly, for that in venereous pustles, there is found a certaine hardnesse at the roote, though outwardly they make shew of choler or bloud. For being opened, you shall finde them stuffed with a certaine plaster-like and tophous matter, or else with tough phlegme, or viscous pus; whence arise these hard tophi, or bony excressences upon the bones, if not from phlegmaticke humours there heaped up and concrete? Fifthly, for that the spermaticke and cold parts doe primarily and principally feele the harme of this disease. Sixthly, for that the ulcers which over-spread the body by meanes of this disease, admit of no cure, unlesse you first cause sweats. Therefore if the matter of the disease, and such ulcers as accompany it were hot and dry, it would grow worse, and be rather increased by a decoction of Quajacum, the roots of China, or sarsaparilla. Seventhly, because oft times this disease, the seede thereof being taken or drawne into the body, so lyeth hid for the space of a yeare, that is shewes no signe thereof, which happens not in diseases proceeding from an hot matter, which causeth quick and violent motions. By this it appeareth that the basis and foundation of the Lues venerea is placed or seated in a phlegmatick humour; yet may I not deny, but that other humours confused therewith may be also in fault, and defiled with the like contagion. For there are scarce any tumours which proceed from a simple humour, and that of one kinde; but as in tumours, so here the denomination is to be taken from that humour which carryeth the chiefe sway.

Chapter IV

Of the Figures of the Lues Venerea

When the Lues venerea is lately taken, maligne ulcers appeare in the privities, swellings in the groines, a virulent strangury runneth oft-times with filthy sanies, which proceeds either from the prostate, or the ulcers of the urethra; the patient is troubled with paines in his joynts, head, and shoulders, and as it were breakings of his armes, legges and all his members, they are weary without a cause, so that neither the foot nor hand can easily performe his duty; their mouths are inflamed, a swelling troubles their throats, which takes away their freedom of speaking and swallowing, yea of their very spittle; pustles rise over all their bodies, but chiefly certaine garlands of them engirt their temples and heads; the shedding or losse of the haire, disgraceth the head and chin; and leanenesse deformeth the rest of the body; yet all of these use not to appeare in all bodies, but some of them in some. But the most certaine signes of this disease are, a callous ulcer in the privities, hard and ill conditioned, and this same is judged to have the same force in a prognosticke, if after it be cicatrized, it retaine the same callouw hardnesse; the Bubo's, or swellings in the groines to returne backe into the body without comming to suppuration, or other manifest cause; these two signes, if they concurre in the same patient, you may judge or foretell that the Lues venerea is either present, or at hand; yet this disease happeneth to many without the concourse of these two signes, which also betrayeth itself by other manifest signes, as ulcers and pustles in the rest of the body, rebellious against medicines though powerfull, and discreetly applyed, unlesse the whole body bee annoynted with Argentum vivum. But when as the disease becometh inveterate, many become impotent to venery, and the malignity and number of the symptomes encrease, their paines remaine fixed and stable, very hard and knotted tophi grow upon the bones and oft-times they become rotten and foule, as also the hands and feete by the corruption of salt phlegme are troubled with chops or clefts, and their heads are seazed upon by an ophiafes and alopecia; whitish tumours with roots deepe fastned in arise, in sundry parts of the body, filled with a matter like the meate of a chesnut, or like a tendon; if they be opened they degenerate into divers ulcers, as putride, eating and other such, according to the nature and condition of the affected bodies. But why the paines are more grievous on the night season; this many bee added to the true reason wee rendred in the precedent Chapter; first for that the venereous virulencie lying as it were asleepe is stirred up and enraged by the warmenesse of the bed and coverings thereof; Secondly, by reason of the patients thoughts which on the night season are wholly turned and fixed upon the onely object of paine.

Chapter V

Of Prognosticks

If the disease be lately taken, associated by a few symptoms, as with some small number of pustles, and little and wandring paines, and the body besides bee young and in good case, and the constitution of the season bee good and favourable, as the spring, then the cure is easie, and may bee happily performed. But on the contrary, that which is inveterate and enraged by the fellowship of many and maligne symptoms, as a fixed paine of the head, knots and rottennessee of the bones ill natured ulcers in a body very much fallen away and weake, and whereof the cure hath beene already sundry times undertaken by Empyricks, but in vaine; or else by learned Physicians, but to whose remedies, approved by reason and experience, the malignity of the disease and the rebellious virulencie hath refused to yeeld, is to be thought uncurable, especially, if to these so many eviles, this bee added, that the patient bee almost wasted with a consumption and hectick leanenesse, by reason of the decay of the native moisture. Wherefore you must onely attempt such by a palliative cure; yet bee wary here in making your prognosticke, for many have been accounted in a desperate case, who have recovered; for by the benefit of God and nature, wonders ofttimes happen in diseases. Young men who are of a rare or laxe habit of body are more subject to this disease, than such as are of a contrary habit and complexion. For as not all who are conversant with such as have the Plague, or live in a pestilent aire, are alike affected; so neither all who lye or accompany with such as have the Lues venerea, are alike infected or tainted. The paines of such as have this disease, are farre different from the paines of the Gout. For those of the Gout returne and torment by certaine periods and fits, but the other are continuall and almost alwaies like themselves; Gouty paines possesse the joynts, and in these condense a a plaster-like matter into knots; but those of the Pocks are rather fastened in the middest of the bones, and at length dissolve them by rottennesse and putrefaction. Venereous ulcers which are upon the yards are hard to cure, but if being healed, they shall remaine hard and callous, they are signes of the disease lying hidde in the body.

Generally, the Lues venerea which now reigneh is farre more milde and easie to bee cured than that which was in former times, when as it first began amongst us: besides, each day it seemeth to bee milder than other. Astrologers think the cause hereof to bee this, for that the coelestiall influences which first brought in this disease, in successe of time by the contrary revolutions of the Starres, lose their power and become weake; so that it may seeme somewhat likely, that at length after some few years it may wholly cease; no otherwise than the disease termed Mentagra, which was very like this in many symptoms, and troubled many of the Romans in the raigne of Tiberius; and the Lichen, which in the time of Claudius (who succeeded Tiberius) vexed not onely Italy, but all Europe besides. Yet Physicians had rather take to themselves the glory of this lesse raging disease, and to referre it to the many and wholsome meanes, which have been invented, used and opposed thereto by the most happy labours of noble wits.

Chapter VI

How Many, and What Means There Are to Oppunge This Disease

Many sorts of remedies have beene found out by many to oppugne and overcome this disease. Yet at this day there are onely foure which are principally used. The first is by a decoction of Quajacum; the second by unction; the third by emplasters, and the fourth by fumigation; all of them by Hydrargyrum, the first excepted. Yet that is not sufficiently strong and powerfull; for experience hath taught, that the decoction of Quajacum hath not sufficient strength to extinguish the venome of the venereous virulency, but onely to give it ease for a time; for because it heates, attenuates, provokes sweate and urine, wastes the excrementitious humours by drying them, it seemeth to cure the disease, for that thereupon, for some time, the paine and all other symptomes seeme more remisse; but these endeavours are weake and deceitfull, as whereby that only which is more subtle in the humours in fault, is exhausted and dispersed by sweat. But Hydrardyrum, as a certaine higher power, conteines therein all the power of Quajacum, yet much more excellent and efficacious; for besides that it heats, attenuates, cuts, resolves and dryes, it provokes sweat and urine, and besides it expels noxious humours upwards and downewards, by the mouth and stoole. By which evacuations not onely the more subtle, but also the more grosse and foeculent excrements, wherein the seat of this disease is properly fixed, are dispersed and evacuated; by which the Physician may bee bold to assure himselfe of certaine victory over the disease. But after the use of the decoction of Quajacum, fresh paines and knots arise by the reliques of the more grosse and viscious humours left in the cavities of the entrailes; but Hydrardyrum leaves no reliques behind it.

CHAPTER VII

HOW TO MAKE CHOICE OF THE WOOD QUAJACUM

That is preferred before the rest, which is of a great logge, of a dusky colour, new, gummy, with a fresh strong smell, an acride and somewhat bitting taste, the barke cleaving very close to the wood. It hath a faculty to heat, rarifie, attenuate, attract, to cause sweat, and move urine, and besides by a specifick property to weaken the virulency of the Lues Venerea. There are three substances taken notice of in this wood: The first is the barke, the other is a whitish wood which is next to the barke, the third is the heart of the wood, that is, the inner, blackish, and more dusky part thereof. The barke is the more dry, wherefore you shall use it when as you would dry more powerfully; the middle substance is more moist, because it is more succulent and fat; that which lyeth betweene both is of a milde temper. Wherefore the two last are more convenient for delicate natures and rare bodies, which require lesse drying. Furthermore, the barke must be given to dense and strong natures, that by the more fierie force thereof, the humours may be made more fluide, and the passages of the body more passable. But I would here bee understood to meane such barke as is not putride and rotten with age, to which fault it is very subject, for that long before it bee shipped by our people, the wood lyeth in heapes upon the shore in the open aire, until they can finde chapmen for it; which, when it is brought aboard, it is stowed in the hold or bottome of the ship, where beneath by the sea through the chinkes of the bords, and above by the mariners, it usually gathereth much dirt. When it is brought hither to us, it is bought and sold by weight, wherefore that it may keep the weight the Druggists lay it up in vaults and cellars under ground, where the surface thereof bedewed with much moisture can scarce escape mouldinesse and rottennesse. Wherefore I doe not like to give the decoction either of the barke or wood which is next thereto to sicke people.

(*To be continued.*)

Abstract of Current Syphilis Literature

It is the purpose of this JOURNAL to review so far as possible all literature on syphilis as it appears in other medical periodicals and to present it in abstract form. Authors are requested to send abstracts or reprints of their papers to the Associate Editor, Dr. Grayson E. Tarkington, Dugan-Stuart Bldg., Hot Springs National Park, Ark.

GRAYSON E. TARKINGTON, M.D., EDITOR.

The Effect of ''Arsenic-Fastness'' of Trypanosoma Equiperdum on the Ratios Between the Parasiticidal Values of Arsphenamine and Neoarsphenamine.—G. C. Lake, United States Public Health Service. Public Health Reports, 1923, vol. xxxviii, p. 1347.

The minimal effective doses of a single lot each of arsphenamine and neoarsphenamine have been determined for three ''arsenic-fast'' strains of Tr. equiperdum and for one nonarsenic-fast, ''normal,'' or possible arsenic-susceptible strain. All four strains were substrains from the same common strain. With the ''arsenic-fast'' strains the minimal effective dose for this arsphenamine and neoarsphenamine was found to be about the same and not far from 50 mg. per kilo, whereas with the ''normal'' strain the minimal effective dose for the same arsphenamine was found to be between 3 and 4 mg. per kilo, and for the same neoarsphenamine about 12 mg. per kilo. No explanation is apparent as to why an ''arsenic-fast'' strain should be proportionately less resistant to arsphenamine than to neoarsphenamine.

Late Results in the Treatment of Syphilis.—H. H. Hazen, Washington, D. C. The Journal of the American Medical Association, 1923, vol. lxxx, p. 1838.

There are no satisfactory criteria as to the cure of syphilis. The relapses may occur after a patient has remained asymptomatic and Wassermann negative for six or seven years. Not all cases of early chancre are cured by modern methods of treatment. In certain instances it is possible that the early and intensive administration of arsphenamine may prevent a patient from developing a natural immunity, and a relapse will occur very shortly after treatment is discontinued. From this it might be argued that treatment should not be begun within the first few days of the appearance of a chancre, but the majority of syphilologists would undoubtedly contend that treatment should be instituted at once, with a view of preventing the possible spread of the disease. Cerebrospinal syphilis can develop by the time the chancre is manifest. Every patient should have a routine spinal puncture done, preferably just before the second course of arsphenamine is administered. A provocative Wassermann reaction may be misleading. It may be distinctly dangerous to the patient, in that a relapse may follow it. It is certain that insufficient treatment could produce the same results. A luetin reaction done under proper precautions may be of some value as a criterion of cure. The results of treatment in early secondary syphilis are surprisingly good. Arsphenamine alone may effect a cure. Apparently arsphenamine is more important than mercury in effecting a cure, for there has been a much higher percentage of cures when two courses of arsphenamine were employed than when but one course was used. A few cases of late syphilis can be cured, occasionally by a small amount of treatment. In the vast majority of instances, late syphilis cannot be cured. Apparently, in some instances, syphilis is a mild infection and is readily cured; in other instances, it is a severe infection and cannot be cured. Intraspinal therapy will often yield results when intravenous therapy fails. Syphilis is not a benign disease. Many deaths are due to it either directly or indirectly.

Neurosyphilis in the Aged.—A. E. Bennett, Philadelphia. Archives of Neurology and Psychiatry, 1923, vol. x, p. 324.

Cerebrospinal syphilis and tabes dorsalis developing in senility (60 years or older) are rare because in most cases the chancre is contracted in early life. The incidence is approximately 0.5 per cent of all neurosyphilis cases. Aged patients suffering from cerebral arteriosclerosis, senile deterioration or nephritis are at times mistaken for neurosyphilitics. Cases developing after 60 years usually have the initial sore in middle life. In a few instances there appears to be a long period of latency, then, in the metamorphosing stage, this immunity is broken down, probably as a result of the degenerative processes of age. Then the neurosyphilitic involvement becomes apparent, and, as a rule, does not respond to treatment, but is rapidly fatal. General paralysis developing in senility is rare, 0.62 per cent, and frequently is confused with senile dementia. General paralysis practically never develops after 65 years. We agree with Herschmann that general paralysis in seniles simulates closely the dementia of senile deterioration. The termination in senile cases is hastened approximately 50 per cent.

Studies on the Cerebrospinal Fluid with an Acetic Anhydride Sulphuric Acid Test. Boltz, Wards Island, N. Y. The American Journal of Psychiatry, 1923, vol. iii, p. 111.

The acetic anhydride-sulphuric acid test is 100 per cent positive with spinal fluids from cases of general paresis. Among psychiatric cases, the acetic anhydride-sulphuric acid test was found positive predominately in cases with neurosyphilis. The more advanced and active the syphilitic condition of the central nervous system, the more positive will be the acetic anhydride-sulphuric acid test reaction. In syphilitic clinics, the test may prove to be valuable in the prognosis of neurosyphilis. In psychoses not due to or complicated with syphilis, and of a functional nature, the acetic anhydride-sulphuric acid test is negative. The author is not fully convinced that the acetic anhydride-sulphuric acid test is specific for neurosyphilis, but it is more apt to be evidence of the destructiveness of the spirocheta pallidum on nervous tissue—more an index of degenerate nerve tissue. The acetic anhydride-sulphuric acid test differentiates two groups of tabetics, one giving a negative reaction, the other showing a slightly positive reaction. In four cases of neurosyphilis with a negative spinal fluid Wassermann, the acetic anhydride-sulphuric acid test was positive.

Biologic Reactions of Arsphenamine.—Jean Oliver, Ethel Douglas and Frank Kolos, San Francisco. Archives of Dermatology and Syphilology, 1923, vol. viii, p. 359.

Gelatin arsphenamine is somewhat less trypanocidal *in vitro* than disodium arsphenamine. Gelatin arsphenamine is retained in the animal at a higher concentration for a longer period than is disodium arsphenamine. Gelatin arsphenamine is as effective as disodium arsphenamine in the treatment of experimental trypanosomiasis and rabbit syphilis. Under certain conditions it is more effective. Therapeutic indexes established on the basis of the late or chemical toxicity of the two preparations favor gelatin arsphenamine as compared to disodium arsphenamine. The immediate toxic effects of disodium arsphenamine may be avoided under experimental conditions by the use of gelatin arsphenamine without any sacrifice in therapeutic efficiency.

Syphilis of the Uterus and Adnexa.—Portis, Chicago. Surgery, Gynecology and Obstetrics, 1923, vol. xxxvii, p. 37.

Syphilis of the body of the uterus is rare. For most of the lesions which have been described as luetic, the specific character has not been definitely established and appears doubtful. Gummata have been reported; these lesions may probably be accepted as luetic, in spite of the fact that treponemas have have not been demonstrated in them. A case of early diffuse syphilitic involvement of the body of the uterus is described. The character of the process was established by the presence of the specific organism in the cellular tissue which separates the muscle bundles. The lesion of the body was apparently secondary to a chancre of the cervix. Involvement of the body probably occurred by direct interstitial invasion from the primary lesion. Adnexal lesions, the syphilitic character of which has been definitely proven, are even rarer than those of the body of the uterus. Chronic vascular and diffuse fibrotic processes have been reported as of luetic origin, but most of these must be excluded because of lack of evidence. In the case reported, a corpus luteum and the surrounding stroma of the ovary were the seat of lymphocytic infiltration. Treponemas were present in this tissue, establishing the specific character of the inflammatory process. That the involvement of the body of the uterus and of the ovary occurred early is indicated, not only by the cellular character of the inflammatory reaction, but also by the development of typical secondary cutaneous syphilides 7 weeks after the onset of the first local symptoms. The blood Wassermann reaction was strongly positive when the skin lesions appeared.

The age of the patient, a previously normal childbearing history, vaginal bleeding, and the gross appearance of the cervix on direct visual examination led to a diagnosis of epithelioma of the cervix.

Cerebral Syphilis.—Brush, Santa Barbara, California. California State Journal of Medicine, 1923, vol. xxi, p. 212.

As compared to tabes and general paresis, cerebral syphilis is an early involvement of the central nervous system. In the former the time that elapses from infection to development of symptoms is rarely less than ten years, in the latter the time is from three to five years. The onset of cerebral syphilis is often acute with headache, cranial nerve involvements, etc., and a mental reaction that is fairly characteristic. The Argyll-Robertson pupil occurs in fifty per cent to seventy-five per cent of all cases of paresis, and in seventy-five per cent to eighty per cent in tabes; its presence in cerebral syphilis is sufficiently rare to make it a differential point of importance. Little value can be placed on the reflex changes. Ninety per cent of paretics have a positive Wassermann reaction in the blood and spinal fluid. Ninety per cent of tabetics have a positive reaction in the spinal fluid, but only 75 per cent have a positive reaction in the blood. In cerebral syphilis the blood and spinal fluid may or may not be positive. The acute cases are the ones most liable to have the positive reactions. A greatly increased globulin content and a high cell count point to cerebral syphilis. Arsenical treatment with the assistance of mercury compounds is indicated.

Arsphenamine vs. Neoarsphenamine, with a Report of 1,609 Injections.—Edward Lester Merritt, Fall River, Mass. The Military Surgeon, 1923, vol. liii, p. 259.

Neoarsphenamine is as valuable a therapeutic agent as arsphenamine. A reaction of some sort, although often slight, is to be expected in from one-third to one-fifth of all injections. Neoarsphenamine is not as toxic as arsphenamine. Neoarsphenamine, because of the fact that it can be used in such small dilution, causes less shock to the patient, and is thus more to be desired than arsphenamine.

Bismuth in the Treatment of Syphilis.—Lawrence K. McCafferty, New York. Archives of Dermatology and Syphilology, 1923, vol. viii, p. 469.

The immediate action of bismuth in primary and secondary syphilis is as effective as that of arsphenamine, although it is slower in its action, both clinically and serologically. There seems to be a real indication for bismuth in Wassermann-fast patients, as well as in patients who have an idiosyncrasy to arsenic. Central nervous system syphilis gives evidence of responding to bismuth as well as it does to intravenous injections of arsphenamine, but the time has been too short to draw any definite conclusions. Stomatitis and local pain from injections are negligible factors. Arsenic, bismuth, and mercury may be used in treating syphilis, either in combination or separately. Routine urinalysis should be made every month.

Application of the Warthin-Starry Silver-Agar Method to the Demonstration of Spirochaeta Pallida in the Spinal Fluid by means of Coagula Obtained by the Alzheimer Method.—Alfred Scott Warthin, Ruth C. Wanstrom and Estella Buffington, Ann Arbor, Mich. Archives of Dermatology and Syphilology, 1923, vol. viii, p. 461.

Staining of sections of spinal fluid coagula by the Warthin-Starry methods offers a valuable means for the demonstration of spirochetes in spinal fluid, serums or other fluids in which the organisms may be present, either in small or large numbers, but especially in the former case.

Syphilis of the Stomach.—Joseph W. Larimore, St. Louis, Mo. Surgery, Gynecology and Obstetrics, 1923, vol. xxxvii, p. 133.

Gastric syphilis manifests a variable symptomatology, a chemistry, and x-ray findings that cannot consistently be of other well-recognized gastric disease. The presence elsewhere of other undoubted signs of syphilis is a very large support to the diagnosis of syphilis of the stomach, and when absent great care must be used in making that diagnosis. Successful medical treatment is diagnostic only in early syphilis. Restoration to normal gastric motility cannot be expected in well-advanced gastric syphilis. The clinical response to antiluetic treatment will not then be helpfully diagnostic. Surgery is indicated in late cases with permanent impairment of the gastric motor function. It is indicated by the clinical course and by the x-ray findings. Resection of the prepyloric stomach is the preferred operation.

Gastric Syphilis; A Report of Two Cases Proved Anatomically.—Wm. A. Brams, Chicago and Karl A. Meyer, Chicago. Surgery, Gynecology and Obstetrics, 1923, vol. xxxvii, p. 127.

The clinical evidence of gastric syphilis consists of pain in the epigastrium, low acidity, marked emaciation, history or evidence of luetic infection, and a good result with specific treatment. To this should be added that the patient is often under the usual age for carcinoma, and that the course is often over a period of years. The anatomic features are multiple, irregular ulcers; thick submucosa; vascular changes; miliary gummata; perivascular infiltrate; and diffuse infiltrate, in which the predominating element is the lymphocyte.

A Case of Syphilis of the Stomach.—Weitzner, New York City. The American Journal of Roentgenology and Radium Therapy, 1923, vol. x, p. 537.

A patient sixty-one years old begins to complain of gastrointestinal symptoms. Roentgenologic examination discloses the presence of a neoplasm of the stomach, which might readily be considered of malignant nature. Its luetic nature was proven by the four plus Wassermann reaction, and the rapid restoration of the stomach to normal, following active antisyphilitic treatment.

Treatment of Syphilis by Bismuth Salts.—Crivelli, Melbourne, Australia. The Medical Journal of Australia, 1923, vol. ii, p. 8.

Given by intramuscular injection with the usual precautions of asepsis, it is painless, non-toxic and immediately powerful in its action. Its local reaction is transient and consists in a slight stiffness of the muscle. It has no general reaction. After a single injection ulcerations and enlarged glands are often reduced in a few days and rapidly disappear with further treatment. Saturation is announced by a very benign stomatitis, resembling mercurial stomatitis, with a blue line along the gums and patches on the cheeks. Five cases reported. In all of these improvement was satisfactory.

Pathological Changes in the Kidney in Congenital Syphilis.—Ernesto De Souza Campos, Baltimore. Johns Hopkins Hospital Bulletin, 1923, vol. xxxiv, p. 253.

A microscopic examination of the kidneys from sixty-nine cases of congenital syphilis showed histologic changes in this organ in every case. These histologic changes were observed in the interstitial tissue and, to a lesser degree, in the parenchymatous apparatus. The interstitial changes which were observed in every case consist principally of a cellular infiltration around the blood vessels of the cortex of the kidney. These changes were very pronounced in forty-three cases, conspicuous in eighteen, and slight in eight. The medullary zone of the kidney is rarely affected and then in very slight degree. Only in seven out of sixty-nine cases were a few collections of cells observed and then principally near the cortex. The pelvis of the kidney is frequently infiltrated with cells which have the same structure as those seen around the blood vessels. The capsule of the kidney shows only a slight infiltration in a few cases. The cells of the infiltration of the kidney in congenital syphilis are similar in structure to the bone marrow cells, namely, they are nongranulated myeloid cells (myeloblasts of Schridde and Naegeli, leucoblasts of Pappenheim, hemocytoblasts of Ferrata), neutrophilic and eosinophilic myelocytes, normoblasts and megalocaryocytes (the last observed in eight specimens). These perivascular myeloid cells found in the kidney, in congenital syphilis, seem to have an autochthonous origin, as they show numerous mitotic figures; this fact may be explained on the basis of the extravascular origin of the granulocytes. The formation of the myeloid tissue in the kidney, in congenital syphilis, seems to be stimulated by the presence of spirochetes, because the latter are seen lying in greater numbers in the interstitial tissue of the organ, mainly around the blood vessels. The perivascular myeloid cells offer great resistance to autolysis, thus permitting the microscopic picture of congenital syphilis of the kidney to be seen even in rather advanced maceration. This fact is important for the anatomic diagnosis of congenital syphilis, because premature babies are often brought for autopsy in a more or less advanced stage of maceration. Parenchymatous lesions in the kidney in congenital syphilis, are practically observed only in infants who have had an extrauterine life and becomes more pronounced as the infants become older. Perhaps it is due to the functional activity of the organ. The kidney in congenital syphilis is retarded in its development. This fact is demonstrated by the presence of the ''neogenic zone'' in kidneys of full-term, stillborn, syphilitic babies, while this is not to be observed in kidneys of normal, full-term, stillborn infants.

Congenital Syphilis of the Nervous System.—Speidel, Louisville. Archives of Pediatrics, 1923, vol. xl, p. 554.

The mother became pregnant and was infected with syphilis at the same time, or at least during the same month. She was given intensive treatment with salvarsan and mercury by a competent syphilographer during the entire period of gestation. Her child, born at term, was apparently normal, but developed syphilitic hemiplegia at the age of 21 months. A severe fright was responsible for bringing to light the hitherto latent congenital syphilis of the nervous system. The child was clinically cured and serologically improved by one year's treatment. Treatment is being continued.

Syphilis of the Orbit.—Jarold E. Kemp, Baltimore. Archives of Dermatology and Syphilology, 1923, vol. viii, p. 165.

Four cases of orbital syphilis are reported and the literature reviewed. Attention is directed to the characteristic syndrome of nocturnal pain, unilateral exophthalmos, pain on pressure over the affected bulb, paralyses of extraocular muscles, disturbances of vision, and sensory disturbances in the distribution of the first or second branches of the trigeminal nerve. The differential diagnosis, prognosis and results of treatment are discussed.

A Study of Serum Flocculation Reactions in Syphilis with Special Reference to the Meinicke, Sachs-Georgi, Kahn and Vernes Reaction.—Max H. Strumia, Philadelphia. Archives of Dermatology and Syphilology, 1923, vol. viii, p. 50.

Precipitation tests in syphilis are technically simpler than the complement-fixation test and more economical in respect to the materials required; but they are subject to error, yielding both falsely negative and falsely positive reactions, although most of them do this in a very small percentage of cases. They are sometimes difficult to read, especially borderline reactions. Studies with four precipitation tests showed an agreement in results with a complement-fixation reaction in from 82.7 to 90 per cent of serums. While a precipitation test may sometimes yield a positive reaction in primary and latent syphilis when the complement-fixation reactions are negative, in general terms, some of the precipitation tests are less sensitive than the latter, and some are more sensitive. A single precipitation test should never be relied on for the serum diagnosis of syphilis. At least two tests should be made in parallel, and the result carefully interpreted. For this, the combination of the Meinicke with the Sachs-Georgi reaction appears to be one of the more reliable methods, but the precipitation tests are best used in connection with a complement-fixation reaction, not only as a control, but as an integral part of the serodiagnosis of syphilis. For this purpose, the Vernes direct method, the Meinicke (third modification), Sachs-Georgi and Kahn method with cholesterinized antigen can be recommended. The Vernes indirect method alone or corroborated by the direct method can be relied on, as well as any of the complement-fixation tests. The value of the precipitation tests must be determined, not only by comparing them with the complement-fixation test, but by accurate and careful study of each case in order to determine exactly the clinical diagnosis.

The Kahn Precipitation Test for Syphilis.—Janet A. Holmes, St. Louis. The Journal of the American Medical Association, 1923, vol. lxxxi, p. 294.

The results in the 1,000 cases show a very close correlation between the Wassermann and Kahn tests, with the balance in favor of the Kahn, the latter showing a greater sensitivity, especially in treated cases. The Kahn test has the further advantage, in that anticomplementary serums give a normal reaction in the precipitation test. Attention, however, should be drawn to the fact that in the Kahn test it is necessary that all serums be absolutely clear. Any fat, for instance, and even slight hemolysis of the serum makes reading difficult. The necessity for care in the mixing of antigens to prevent spontaneous precipitation in nonsyphilitic serums must not be overlooked. But, as the case stands, the outlook for the Kahn test seems most favorable, and with more work on the standardization of antigens, we may hope in the future for a test that will relieve the laboratory of the intricacies of the Wassermann reaction.

The Wassermann Reaction in Leprosy.—John A. Kolmer and Oswald E. Denney, Philadelphia. Archives of Dermatology and Syphilology, 1923, vol. viii, p. 63.

In a series of 159 cases of leprosy, clinical or serologic evidence of syphilis was found in twenty-seven, or 17 per cent. In nonsyphilitic lepers, the Wassermann reactions by a new technic were uniformly negative. With an old technic similar to the original Wassermann method, apparently falsely positive reactions occurred with 7.2 per cent of serums. In some cases of leprosy, there is an increased tendency of the serum to yield falsely positive Wassermann reactions; this is especially true in tests employing alcoholic extracts of tissue saturated with cholesterol. In the new complement-fixation test for syphilis, this tendency is neutralized by the use of a new antigen largely free from anticomplementary activity and other technical improvements. Since the new complement-fixation reaction does not yield falsely positive reactions in leprosy, it is of value in differential diagnosis between cases simulating both leprosy and syphilis. A positive reaction in leprosy with the new method justifies the clinician in proceeding with antisyphilitic treatment without the mental reservation that he may be uselessly subjecting a leper to unnecessary or even harmful measures.

Biologic Reactions of Arsphenamin.—Oliver and Douglas, San Francisco. Archives of Dermatology and Syphilology, 1923, vol. vii, p. 778.

The plasma proteins, especially the globulins, form compounds with arsphenamine both *in vitro* and *in vivo.* The arsphenamine content of these compounds varies with the H-ion concentration. Under physiologic limits of H-ion concentration, only traces of inorganic arsenic are found. Other hydrophilic colloids, such as gum arabic and egg albumen, react in a similar way with arsphenamine and inorganic arsenates. The protection afforded by hydrophilic colloids against the agglutination of red blood cells by arsphenamine is due to the union of the former with the latter, thus preventing the binding of the arsphenamine by the cells. This is the physiologic method of protection which operates after the administration of therapeutic doses. The change in the coagulation properties of the plasma proteins after the injection of arsphenamine may be explained by the assumption that the compound with arsphenamine is soluble at certain H-ion concentrations.

Biologic Reactions of Arsphenamin.—Jean Oliver, So Sabro Yamada and Frank Kolos, San Francisco. Archives of Dermatology and Syphilology, 1923, vol. viii, p. 1.

The combination of arsphenamine with hydrophil colloids reduces the toxicity of the drug. Gelatin is the most effective in this regard of the colloids examined. The decrease in toxicity is a general one as shown by the facts that: (a) The physical toxicity of arsphenamine is removed; (b) The chemical toxicity is reduced to three-fifths; (c) The circulatory disturbances following its administration are markedly lessened.

The Precipitation Test for Syphilis of Concentrated Arachnoid Fluid and Serum.—Russel D. Herrold, Chicago. The Journal of the American Medical Association, 1923, vol. lxxxi, p. 203.

The ring or contact precipitation test for the diagnosis of syphilis has been successfully applied to the arachnoid fluid by means of a single and practical method of concentration. This is accomplished by adding a saturated solution of ammonium sulphate to the fluid, and redissolving the precipitate in physiologic sodium chloride solution in a quantity equal to a fractional amount of the original fluid. The euglobulin fraction has been found to contain almost all of the syphilitic antibody or ''reagin'' in serum, as indicated by the precipitation and Wassermann tests of solutions of fractional precipitates obtained by the ammonium sulphate method. The precipitated fraction containing the ''reagin'' in serum may be dissolved in physiologic sodium chloride solution in amounts much less than the original quantity of whole serum, and, thus concentrated, it gives a more sensitive test than the whole serum. A practical method for routine use has been described and applied to a series of 100 cases, the majority being in patients treated for syphilis in most of whom the serum was either weakly positive or negative on Wassermann tests of the whole serum; and the results in this series indicate that the method of concentration and ring precipitation gives a more sensitive test than reactions with whole serum. The method outlined may prove a valuable aid in the control of treatment.

Rapid Precipitation Phase of the Kahn Test for Syphilis.—R. L. Kahn, Lansing, Mich. The Journal of the American Medical Association, 1923, vol. lxxxi, p. 88.

The original procedures of the precipitation test for syphilis proposed by the author possess two important limitations: 1. The weaker serums require overnight incubation to bring forth precipitates; 2. Occasionally, serums from active syphilis give negative reactions although employing a presumably sensitive antigen. A procedure is presented in this paper which entirely overcomes the first limitation, and practically overcomes the second. At least 95 per cent of the precipitation reactions with the new procedure are completed in from five to ten minutes after mixing serum with the antigen-salt solution mixture, and the final reading is taken after about one hour incubation. Three equal amounts of serum are employed in each test with varying amounts of antigen mixture: The final reaction is essentially one of the following: (1) precipitation with all amounts of antigen mixture; (2) precipitation with the larger amounts of antigen mixture and negative with the small amounts; (3) precipitation with the smaller amounts of antigen mixture and negative with the larger amounts, or (4) no precipitation with all amounts. It is believed that the degree of the reaction with the larger or smaller amounts of antigen mixture is indicative of a definite clinical condition in the patient. Furthermore, experience gained with about 2,000 examinations indicates that there is practically no tendency with this procedure to lose serologic reactions.

Bismuth in the Treatment of Syphilis.—J. G. Hopkins, New York. Archives of Dermatology and Syphilology, 1923, vol. vii, p. 745.

The experiments reported on rabbits show that sodium and potassium tartrobismuthate has marked spirocheticidal power and a curative action on a syphilitic lesion in these animals; that in a single injection it is about as effective as neoarsphenamine and more effective than mercuric salicylate. The observations on early active human cases show that it accomplishes at least a temporary apparent cure. Its effect on latent cases suggests that it may be useful in the treatment of those which are resistant to other drugs. These results are in general agreement with those reported by others and indicate that we have in bismuth a new and powerful antisyphilitic agent. There is as yet no reason to suppose that it will replace other drugs, the efficacy of which has been proven by long experience; and at present the treatment of syphilitic patients by bismuth alone is justifiable only in an attempt to appraise its therapeutic value. Further study of its clinical effect is much needed, but it seems reasonable to hope that better results will be obtained by combined treatment with arsphenamine and bismuth, and probably with mercurials, than by any of these drugs used alone.

Quantitative Studies with Arsphenamine. II. Distribution and Excretion after Intravenous Injection.—A. C. Kolls and J. B. Youmans, Baltimore. Johns Hopkins Hospital Bulletin, 1923, vol. xxxiv, p. 181.

Approximately three-fourths of the arsphenamine injected leaves the blood stream in a few minutes after the completion of the injection. The remaining portion is rapidly reduced in amount, but traces may be found twenty-four hours later. The drug is stored in the liver, spleen, kidneys, lungs, cardiac and skeletal muscle. There is evidence that the alteration or excretion (or both processes, perhaps) has appreciably reduced the amount of drug three hours after injection. The liver is a more important excretory organ for arsphenamine and neoarsphenamine than the kidney. The brain shows a much lower concentration of drug in the experimental animal than does any other organ. The cerebrospinal fluid, during the first twenty-four hours, if it contains the drug at all, does so only in minute concentration, which is too low to estimate with accuracy.

Bismuth in the Treatment of Syphilis. Report of Clinical and Experimental Studies.—Joseph V. Klauder, Philadelphia. Archives of Dermatology and Syphilology, 1923, vol. vii, p. 721.

The report is based on an experimental study of bismuth as a spirocheticidal drug in rabbit syphilis. The relation between the therapeutic active dose and the lethal dose is discussed, as well as the clinical results from the use of bismuth in the treatment of fifty syphilitic patients in the three stages of syphilis, the majority of whom presented a cutaneous manifestation of the disease. The bismuth preparations employed were the French preparation of sodium and potassium tartrobismuthate in aqueous solution and in olive oil, potassium tartrobismuthate in aqueous solution and bismuth trioxid in olive oil and by inunctions. The chemistry of the bismuth tartrates is discussed. All of the bismuth preparations employed in the study were administered intramuscularly. Intravenous administration is positively contraindicated. The doses of the bismuth preparations employed ranged from 0.1 gm. to 0.2 gm., the interval between injections ranged from every other day to every fourth day. The total amount of the bismuth preparations employed that can be well tolerated in a specified time cannot be stated arbitrarily. In this study, this amount ranged from 1 gm. in exceptional cases, to about 2.5 gm. The majority of patients will perhaps tolerate about 2 gm. in one month without developing any untoward reactions. Untoward reactions of bismuth therapy in syphilis are given. A foul breath and a gingival blue line, which forecast the appearance of stomatitis, are particularly stressed. Lesions of primary, secondary and tertiary syphilis were involuted after a total administration of the bismuth preparations employed, in amounts ranging from 0.3 gm. to 1.5 gm. The four plus Wassermann reaction of patients in early secondary and late secondary stages of syphilis became negative, in the majority of cases, following a total administration of about 2 gm. of the bismuth preparations employed. Other patients, however, required 3 gm. or more before the Wassermann test became negative. The four plus reaction of primary syphilis became negative after a lesser amount of the drug, and was somewhat proportional to the duration of the chancre. The four plus Wassermann reaction of tertiary syphilis required varying amounts of bismuth treatment, and cannot be stated arbitrarily. In two patients in the early stage of syphilis, there was an early recurrence of a positive Wassermann reaction after the cessation of treatment. The antisyphilitic effect of bismuth is noted for some time after the administration of the drug. The pain and local reaction following an injection of the bismuth preparations were variable. An aqueous solution of sodium and potassium tartrobismuthate was more painful than an oil suspension. Potassium tartrobismuthate was injected with a local anesthetic—butyn; the pain after injection was negligible. Injections of bismuth trioxide in olive oil were not painful. Knowledge of the distribution of bismuth and its elimination when injected intramuscularly is reviewed. The employment of 50 per cent bismuth inunctions in the treatment of human syphilis exerted a feeble spirocheticidal action. The observations of Sazerac and Levaditi on the spirocheticidal action of bismuth in experimental syphilis were confirmed. The therapeutic active and maximum tolerated doses of the bismuth preparations studied in syphilitic and normal rabbits are given. Bismuth applied in the form of inunctions to syphilitic rabbits exerted a spirocheticidal action. It was not possible in a brief duration of the clinical study to determine the comparative value of the bismuth preparations employed. The three preparations appeared to exert equal spirocheticidal action in the treatment of human syphilis. So far as its spirocheticidal action is concerned, bismuth can be placed about midway between mercury and arsphenamine. Bismuth therapy is particularly advantageous in the treatment of syphilitic patients who are hypersensitive to arsphenamine so that the use of the latter drug is restricted or contraindicted. Neurorecurrence, appearing after irregular and lapsing treatment with the arsphenamines is briefly discussed. Bismuth, by virtue of its exerting a less energetic spirocheticidal action than arsphenamine, does not in all probability inhibit the immunologic reaction of the host to such an extent as it is believed arsphenamine does. One would, therefore, expect a lessened incidence of early neurosyphilis (neurorecidive) following irregular and lapsing treatment with bismuth.

The Colloidal Gold Test of the Spinal Fluid.—P. B. Newcomb, Tucson, Arizona. Southwestern Medicine, 1923, vol. vii, p. 221.

The collodial gold reaction was apparently as reliable as the Wassermann test on the spinal fluid and in some instances, by reason of positive gold curve occurring with negative Wassermann in cases that were clinically luetic, seemed to point to the possible later appearance of a positive Wassermann in the suspected individuals. The author presents the colloidal gold test as a valuable diagnostic procedure in suspected derangement of the central nervous system. There is no one technical method that can be considered as absolutely final, and the unsupplemented colloidal gold test is insufficient evidence upon which to base a diagnosis. The author believes that no cerebrospinal fluid examination for clinical purposes is complete without the use of the gold test.

Congenital Syphilis.—Stewart H. Welch, Birmingham, Ala. Southern Medical Journal, 1923, vol. xvi, p. 417.

The present laboratory procedures are inadequate. Further progress apparently depends upon more laboratory assistance. Therapeutically, congenital syphilis demands every consideration given to acquired syphilis. Activity and infectivity demand active treatment by the route indicated by the degree of activity and infectivity present. The practice of intelligent obstetrics is important in minimizing irreparable damages for the subsequent treatment, and for the possible prevention of congenital syphilis. Intelligently administered, pediatric care is as essential to an infant infected with syphilis as is mercury.

Syphilitic Osteochondritis.—George W. Bowman Indianapolis. Indianapolis Medical Journal, 1923, vol. xxvi, p. 66.

A clinical diagnosis should be made in spite of possible negative laboratory findings. One must not forget the possibility of a negative Wassermann in a positive syphilis, or the greater value of the positive Wassermann. Loss of power or motility in a limb in a patient under six months of age is highly suggestive of syphilis. Early diagnosis and treatment must be instituted before permanent changes result. The roentgenogram is a valuable aid to diagnosis. The condition is due usually to a latent, torpid type of congenital syphilis. The therapeutic test in the face of negative laboratory findings is harmless and effective.

Comparison of the Wassermann Test with the Kahn Flocculation Test in 1,000 Cases.—Litterer, Nashville. The Journal of the Tennessee State Medical Association, vol. xvi, p. 132.

The agreement with the Wassermann reaction was surprisingly accurate considering its simplicity, economy of materials and time. The test or its modification may be used to advantage in checking up the Wassermann reaction especially in doubtful cases. The author does not feel that the test should supplant the Wassermann reaction, but is of the opinion that that two should be run conjointly to insure more accurate reports. It certainly deserves serious consideration on the part of serologists.

Syphilis Among the Insane—Further Observations.—George L. Echold, Milledgeville. Ga. The Journal of the Medical Association of Georgia, 1923, vol. xii, p. 103.

In 6 per cent or more of the resident population at the Georgia State Sanitarium the mental disease seems to be directly traceable to syphilis. The male syphilitic is much more liable to neurosyphilitic involvement than the female syphilitic. Our observations show that the colored syphilitic is just as liable to a neurosyphilitic involvement as the white syphilitic. Syphilis of the nervous system is more prevalent than it was formerly thought to be. The most treatable stage of neurosyphilis is certainly the earliest stage, and this early stage is determined definitely by lumbar puncture—vascular type excepted. In treating late syphilis we can only hope to arrest the process. The damages already done cannot be repaired and this is most especially true of the nervous system. Our observations at the Georgia State Sanitarium lead us to think that syphilis in all its forms, and most especially the late forms, is best treated by a judicious combination of salvarsan, iodine of potash and mercury.

The Anticoagulating Action of the Arsenobenzols on Blood.—Thomas Anwyl-Davies, London, and John Mellanby, London. The Lancet, 1923, vol. ccv, p. 555.

The authors have found that some of the arsenobenzols (neosalvarsan, sulfarsenol, novarsenobillon), when added to blood to the extent of 0.1 per cent prevent its coagulation. This inhibition is due to the action of the arsenobenzol on the fibrinogen, probably by direct combination with it. The combination of the arsenobenzol with fibrinogen depends upon the organic grouping, since arsenious oxide has no effect on the coagulability of the blood, nor does arsenobenzol combined with glucose (stabilarsan) alter blood coagulation. Arsenobenzol, 0.1 per cent, inhibits the coagulation of blood not only *in vitro* but also *in vivo*. But in the animal body the inhibition of coagulation passes off within an hour, probably owing to the passage of the arsenobenzol from the blood into the tissues. Therapeutic doses of the various salvarsan preparations intravenously injected into men or women have practically no effect on the coagulability of the blood, since these quantities fall far below the minimum amounts required to produce fluid blood. Further, the arsenobenzols do not appear to accumulate in the blood and thereby affect its coagulability, since even after prolonged courses of administration the coagulability of the blood remains normal. Hence, previous treatment with arsenobenzols, from the point of view of the blood coagulability, need not be seriously considered when surgical operations are in question.

The Treatment of Syphilis with Bismuth.—Joseph V. Klauder, Philadelphia. The Therapeutic Gazette, 1923, vol. xlvii, p. 381.

This report is based upon the clinical results obtained in the treatment of seventy-five syphilitic patients, who were in the three stages of the disease, the majority of whom presented cutaneous manifestations. The bismuth preparations employed were sodium and potassium tartrobismuthate in aqueous solution, luatol, and the same drug in olive oil suspension, trepol. Bismuth trioxide was also employed. The drug was suspended in olive oil and administered intramuscularly and also in the form of inunctions. Spirochetes disappear from the lesions of primary and secondary syphilis twenty-four hours after the administration of 0.2 gm. of the drug. Lesions of primary and secondary and tertiary syphilis involving the skin and mucous membranes involute after a total administration of bismuth ranging in amounts from 0.3 gm. to 1.5 gm. Patients with visceral syphilis and neurosyphilis were not included in this study.

The Intensive Treatment of Early Syphilis.—W. G. Schultz, Tucson, Arizona. Southwestern Medicine, 1923, vol. vii, p. 73.

With very few exceptions all cases of early syphilis will tolerate some form of intensive treatment, and this method of treatment for these cases should occupy a place of first importance. This form of treatment properly managed will lessen the danger of arsenic fixed cases. Our best efforts should be centered on early diagnoses. The intensive form of treatment is a most valuable addition to our therapeutic armamentarium for the careless individual, in that it overcomes some of the dangers he imposes upon himself.

Remarks on the Treatment of Syphilis.—David Lees, Edinburgh. Journal of State Medicine, 1923, vol. xxxi, p. 251.

The earlier the treatment is administered, the greater the prospect of cure. The early period of the disease is the period of greatest transmission and of greatest danger to the community, but it is also the period in which the chance of absolute cure by salvarsan and its substitutes is by far the greatest. When administered intramuscularly the ''914'' compounds are more potent than when given intravenously, and as potent as the ''606'' group intravenously, and there is no immediate untoward effect following on their administration. Discomfort is comparatively small, and is more marked in the sedentary than in the active worker. Sulfarsenol can be employed in the same manner and there is no pain subsequent to its administration intramuscularly. The immediate signs of intolerance to arsenobenzol administration are more alarming than dangerous. Of the late toxic reactions dermatitis and jaundice are the most serious conditions which are met with. The only known methods of avoiding these conditions are careful technic and careful dosage, combined with systematic weight recording of the patient, and thorough examination of the urine for any sign of commencing intolerance, before the drug is administered. In early localized or seronegative syphilis, the arsenobenzol compounds will rapidly sterilize the patient, and their continued administration in sufficient dosage will prevent the Wassermann test from ever becoming ''positive.'' Their administration should be continued in all cases during the succeeding two years, whether there is any clinical or serologic evidence of syphilitic infection or not. It is preferable in all cases of syphilis to overtreat than to undertreat, and very much less dangerous to the patient in the long run.

Studies in Familial Neurosyphilis.—Joseph Earle Moore, and Albert Keidel, Baltimore. The Journal of the American Medical Association, 1923, vol. lxxx, p. 818.

In three families, of which two contained three members each, and one two members, who all acquired syphilis from different sources and at different dates, all developed neurosyphilis. This occurrence can best be explained on the basis of familial predisposition. The clinical and experimental evidence now available does not settle the question as to the existence of a neurotropic strain of Spirochaeta pallida.

Syphilis and Marriage.—Amand Routh, London. The Lancet, 1923, vol. cciv, p. 644.

The association of syphilis and marriage is the cause of more individual, social, and national trouble than any other disease affecting family life.

A Case of Syphilis With Bone Lesions.—David C. Dodds, Albuquerque, N. M. Southwestern Medicine, 1922, vol. vi, p. 154.

The case reported presents little that is not well known. The interest is in the general character of the case; in the history of past positive lesions and in the present lesions; in the question as to whether the case is one of hereditary or of acquired syphilis; and, lastly, in the progress of the case under treatment.

The Problem of the Syphilitic Child.—Margaret Rorke, Glasgow. The Journal of State Medicine, 1923, vol. xxxi, p. 82.

Congenital Syphilis is absolutely possible to stamp out. The treatment of the mother during every pregnancy, followed by the treatment of the child immediately after birth and by its being kept under supervision and treatment at the judgment of a specialist for some years, should make Congenital Syphilis so rare that our students would only be taught from text-books and pictures—we would soon have no cases to show! The preventive treatment of Congenital Syphilis is essentially hopeful. Every child maimed, purblind, deaf, or mentally defective through Congential Syphilis should be considered by an educated public opinion to have been neglected and cruelly used by its parents, in that they failed to prevent these things by proper treatment.

Studies on the Influence of Pregnancy in Syphilis.—Joseph Earle Moore, Baltimore. Bulletin of Johns Hopkins Hospital, 1923, vol. xxxiv, p. 89.

A critical study of the clinical and experimental evidence in the literature shows that in all probability neither Colles' law nor the theory of the paternal transmission of syphilis directly to the fetus are valid. The clinical data supplied by this study of 178 pregnant women with positive blood Wassermann reactions and 22 non-pregnant mothers of syphilitic children support this belief. Forty-four of these women, or 22 per cent, had outspoken lesions of early or late syphilis at the time of admission. Of the remainder, syphilis was proved or strongly suggested by the history, physical examination, response to treatment, or subsequent course, or a combination of these factors, in 72 per cent. In only 21.5 per cent of the total 200 cases, therefore, were all evidences of syphilis (except a positive blood Wassermann) lacking. This study also demonstrates that the factor of pregnancy may cause striking deviations from the usual course of syphilitic infection. If impregnation and infection approximately coincide, or if infection occurs during the course of pregnancy, the patient may develop the usual early manifestations of syphilis which are, however, much milder than if she is infected independently of pregnancy. Of those pregnant patients in whom the probable date of infection could be compared with the type of lesions present, approximately one-half behaved toward infection in this manner. A slightly larger proportion of women, if infected with syphilis at about the time of impregnation, fail to develop any of the usual early lesions of syphilis. Under these circumstances, it is fair to assume that pregnancy is the factor which suppresses the lesions of the disease. In a few patients (in this series, three of 200 women), the response to infection is markedly altered. The usual time relations between primary and secondary syphilis are much prolonged; on the other hand, the interval between early syphilis and tertiarism may be much shortened, and grave lesions of a tertiary type may appear early in the course of the disease. The protection against the early lesions of syphilis afforded by pregnancy may persist over a long period of years, and possible for a lifetime. Spontaneous cure of syphilis seems in a few instances to have been the ultimate result. In those women of this series who developed late syphilis, the viscera, and particularly the cardio-vascular apparatus, were especially prone to involvement; whereas tertiary lesions of the skin or bones and neurosyphilis, either clinical or asymptomatic, were rare. It is shown that in 33 of these 200 patients, the blood Wassermann reaction gave anomalous results. In 10 per cent of the pregnant women with secondary syphilis, the reaction was negative. In the women with latent syphilis, it was prone to vacillate markedly without treatment; and in a number of cases, a negative or positive reaction during pregnancy spontaneously changed to the reverse after delivery. The possible factors responsible for this condition are briefly considered. The nature of the mechanism by which pregnancy causes these alterations in the course of syphilitic infection is unknown. Various possibilities are mentioned.

Diagnosis and Treatment of Syphilis.—W. H. Connor, Lieutenant Commander, Medical Corps, United States Navy. United States Naval Medical Bulletin. 1923 vol. xviii, p. 456.

Syphilis is an infectious disease of extraordinary chronicity attacking any and at times all organs of the body and manifesting itself in diverse ways. Using the Wassermann test it is possible to diagnosis syphilis in all its phases in about 95 per cent of the cases. Today a diagnosis of syphilis could hardly be accepted, no matter how characteristic the signs, without the aid of a properly conducted laboratory. The succession of lesions that usually occur in syphilis have been grouped into the primary, secondary, tertiary, and meta- or para-syphilitic stage. An attempt to classify the late sclerotic changes as quarternary has been suggested, but has not received unqualified support. The signs and symptoms of the primary and secondary periods are well known, but there is such a multiplicity of symptoms in the parasyphilitic conditions that it would be useless to even attempt to enumerate them. In parasyphilitic conditions, however, a careful examination of the eye and its reflexes furnish us with the greatest single amount of information, for even a slight irregularity of the pupil should at once attract our attention, directing us toward a luetic origin. The most important point in lues is the finding of the Spirochaeta pallida, for that only can mean syphilis. They can be found throughout the disease either by dark-field examination, by staining the secretions, or in stained section. A positive spinal Wassermann is more indicative of syphilis than a positive blood Wassermann. The Wassermann serves a two fold purpose: (1) As an invaluable aid in diagnosis and (2) as a guide in treatment. A spinal puncture with examination of the cerebrospinal fluid should be made at the termination of the systemic invasion period even if the patient is symptomless and the Wassermann, which is only a symptom, is negative. If the blood is negative and the spinal fluid shows no organic disturbance at this time and proper treatment is continued, there will probably be no invasion of the cerebrospinal system. In considering the treatment of syphilis we have two definite objects: First, to clear up any symptoms referable to the disease, and second, to clear up the laboratory evidence of the spirochaetae either in the blood or in the spinal fluid.

Asthma and Septicemia and Syphilis.—A Hernandez, Tucson, Arizona. Southwestern Medicine, 1923. Vol. vii, pp. 159.

Luetic people have less resistance to the toxin of the spherical bacteria, and these are exalted by the virulence of the Treponema pallidum. In all septic infections where luetic conditions exist the best results can be expected from the specific treatment. A previous infection with gonococcus appears to give a degree of immunity to the cocci; but when the infection comes from the dental foci or tonsils, where the gonococcus is not present, the patient has no immunity from septicemia; on the contrary, when an infected tooth is removed, sometimes the virus becomes very exalted and produces septicemia and pyemia.

Syphilitic Macular Atrophy.—V. Pardo-Castello, Havana, Cuba. Archives of Dermatology and Syphilology, 1923, vol. vii, p. 465.

A case of cutaneous macular atrophy of syphilitic origin in a colored man, 29 years of age is reported. No other signs of syphilis could be found. The Wassermann reaction was strongly positive. Pathologically, there was degeneration and atrophy of the elastic tissue, hyperplasia of the connective tissue, arthritis, moderate perivascular infiltration and atrophy of the epidermis. This case resembles closely the condition described by Schweninger and Buzzi under the name of multiple benign tumor-like newgrowths. The condition first reported by these authors seems to be a form of macular atrophy of the skin due to different etiologic causes, one of which might be syphilis. The diagnosis of syphilis in this case is based on the history of the patient, the pathologic findings, the strongly positive Wassermann test, and on the fact that after four months of intensive specific treatment no new lesions have appeared.

Frambesiform Syphilide: Herman Goodman and Eugene F. Traub, New York. Archives of Dermatology and Syphilology, 1923, vol. vii, p. 619.

The authors call attention to a rare syphilide, frambesiform syphilide, and report an example in a man who presented most strikingly the accepted features of the manifestations. They have briefly reviewed the textbook descriptions, summarized the opinion of the earlier writers, and extensively reported the discussion of the gentlemen of the Section on Dermatology of the Royal Society of Medicine. They briefly recalled the comparison between syphilis and frambesia tropica, and quoted at length some of the methods used in the experimental laboratory to distinguish the spirochetal diseases, syphilis and yaws, as well as giving some of the differential diagnostic clinical features of the two diseases.

The Early Diagnosis of Syphilis.—Cleveland C. MacLane, Chicago. Medical Review of Reviews 1923, vol. xxix, p. 202.

A definite clinical lesion answering to the pathologic picture suffices for a diagnosis of syphilis. A clouded clinical picture, remote in a possible visible diagnosis, with a strongly positive Wassermann reaction should be accepted as syphilis. A clouded clinical picture with a graded weakly reacting blood test and a tacit admission of previous infection or familial history, with a hard, firm, generalized adenopathy, should be treated as syphilis. An absence of a clinical picture with one or more vague complaints, a negative blood Wassermann reaction, no free admission of infection, no familial trace, refusal of spinal puncture and bladder examination, in the face of no other organic disease and a general response to antisyphilitic medication should be accepted as syphilis or parasyphilis, and the reaction of the organism to the administration of the drug be our diagnostic aid.

The ''Local'' Wassermann Reaction: A New Diagnostic Aid in Primary Syphilis.—D. Stern and Harold Rypins, Minneapolis. Minnesota Medicine, 1923, vol. vi, p. 167.

The ''local'' Wassermann reaction, carried out on the surface sera of chancres in forty-three cases of demonstrated primary syphilis was positive in all cases. It was negative on the sera from five proved non-luetic lesions. Of these forty-three cases of primary chancre, the dark-field was positive in forty-one, or 95.3 per cent, and the blood Wassermann in thirteen, or 30.2 per cent. Treatment of the lesions with anti-spirocheticide, even when the spirochetes have disappeared, does not interfere with the reaction. In cases where no dark-field is available, or where the dark-field is negative, the ''local'' Wassermann reaction is the only method for making a positive diagnosis of primary chancre. The ''local'' Wassermann is a simple and practicable diagnostic procedure in primary chancre, and the reliability of the results obtained is comparable to those obtained by the dark-field microscope.

Concerning the Specificity of Cholesterinized Antigens in the Serologic Diagnosis of Syphilis.—Robert A. Kilduffe, Pittsburgh. Archives of Dermatology and Syphilology, 1923, vol. vii, p. 363.

Cholesterinized extracts are much more sensitive than alcoholic extracts or acetone-insoluble lipoids as antigens in the performance of complement-fixation reactions in syphilis. Without the use of cholesterinized antigens, either a diagnosis will be missed or treatment prematurely interrupted in a definite and relatively high number of cases. Nonspecific fixation with a carefully titrated cholesterinized antigen is much less frequent than has hitherto been supposed and may be looked on as relatively rare. No syphilitic person should be dismissed from treatment while fixation in any degree can be secured with a cholesterinized antigen. Plus two to plus four fixations with such antigens may be looked on as strongly presumptive evidence of the presence of syphilitic reagin. Cholesterin-plus reactions should not be dismissed in a routine manner as nonspecific, but should form the starting point of an exhaustive clinical and laboratory survey without which the possibility of syphilis cannot be summarily dismissed. A thorough, exhaustive and extensive study of cholesterin-plus reactions is indicated in order that there may be a concerted clinical and laboratory opinion as to their exact status in the serologic diagnosis of syphilis.

Observations on the Precipitin Reaction for Syphilis.—Willson B. Moody, Omaha. The Journal of the American Medical Association, 1923, vol. lxxx, p. 383.

Fifteen hundred serums were studied. Complete agreement occurred in 1,483 serums, the Wassermann reaction was positive and the precipitin negative in fourteen instances, and the Wassermann was negative and the precipitin positive in three. In three instances in which the Wassermann was positive and the precipitin negative, the tests were repeated and the reactions found to agree, (positive). In one case, the Wassermann was negative and the precipitin positive, and at necropsy syphilitic aortitis with aneurysm was found. In one instance with repeated tests, the Wassermann was always positive, and at no time could any trace of precipitation be made out.

A Wassermann Micro-Technic Needing only Occasional Titration of the Complement.—Robert Donald, London. The British Journal of Dermatology and Syphilis, 1923, vol. xxxv, p. 50.

The special feature of this method is to use in the successive batches of tests complement of known suitable titre from an ear vessel of one or more duly titrated cavies, which cavies with good treatment will do service for at least a couple of years. Standardization of the Wassermann test is largely secured by the use of a succession of various only-once-used complements from donors that can give no more. ''Of all the reagents in the

Wassermann reaction, complement is the least capable of standardization, and it is certainly the reagent which is most often responsible for discrepancies in the results on different occasions.'' Incidentally the use thus of an already titrated cavy saves about ninety minutes per batch of tests. The involved standardization of the red-cells suspension is easily carried out by hemoglobinometer. The article has a necessarily detailed account of the ''hall-marked'' drop-measuring micro-technic, by means of which was worked out the feasibility of thus using repeatedly a titrated cavy. The micro-technic furnishes most simply, cheaply and compactly a supply of sterile individual measuring-pipettes for the sera to be tested. The sera are taken sterile from a pricked capillary area coated with sterile paraffin wax. Important among the details of technic is a simple harmless instantaneously heat-etching ink for inactivating-pipettes.

Clinical Experience with Kolmer Complement-Fixation Test for Syphilis.—Jay Frank Schamberg and S. S. Greenbaum, Philadelphia. The Journal of the American Medical Association, 1923, vol. lxxx, p. 836.

The Kolmer complement fixation test is distinctly more sensitive than the routine three antigen method. With its employment, the serums of syphilitic subjects are slower in becoming negative, thus insuring more adequate treatment. The test detects relapsing positives at an earlier period than the older method. The quantitative character of the test enables the physician to determine more accurately the serologic status of the patient, and to gage the influence of treatment. In a fairly large experience the authors have never observed a false positive by the Kolmer test. They regard the Kolmer test as an invaluable advance in the serologic study of syphilis.

The Inability of Serum with a High Cholesterol Content to Increase the Strength of the Wassermann Reaction.—William Thalhimer and Beatrice M. Hogan, Milwaukee. Archives of Dermatology and Syphilology, 1923, vol. vii, p. 482.

This investigation demonstrates that when relatively large amounts of a high cholesterol serum are added to the Kolmer quantitative test, no increase in the strength of the reaction occurs. The authors believe that this indicates that hypercholesterolemia does not increase the strength of the Wassermann reaction whether plain or cholesterolized antigens are used. Their experiments also demonstrate that hypercholesterolemia does not cause a falsely positive (nonspecific) Wassermann reaction.

Unusual Wassermann Report in a Non-Syphilitic Case.—C. J. Broeman, Cincinnati, Ohio. The Cincinnati Journal of Medicine, 1923, vol. iv, p. 144.

A positive Wassermann reaction does not always mean that a syphilitic infection is present. The blind dependence which so many physicians are now placing upon this blood test is a very dangerous state of mind, and efforts should be made to correct it. A "four-plus Hecht-Weicht-Weinberg-Gradwohl" does not invariably "mean syphilis" yet this statement is repeatedly made without any protest from physicians. Valuable as the Wassermann reaction undoubtedly is, it is not uniformly infallible, and there should be a more wide-spread comprehension of this situation than at present prevails.

The Wassermann Test.—David L. Belding, Boston. The Boston Medical and Surgical Journal, 1923, vol. clxxxviii, p. 692.

In routine obstetrical examinations comparatively few women with positive Wassermann tests show clinical signs of syphilis. Syphilis is an appreciable factor in the causation of fetal deaths, directly or indirectly producing from 30 to 40 per cent. Syphilis has a similar effect upon the mortality of children during the first years of life. The offspring are more seriously affected when syphilis in the mother is clinically evident, and when the reaction is a strong rather than a weak positive. A positive Wassermann test in the absence of clinical findings, especially if repeatedly positive, should not be disregarded. With cholesterolized antigens, positive reactions in pregnant women may be obtained in non-syphilitics. Untreated mothers with histories of clinical syphilis and positive Wassermann tests may produce as high as 60 per cent of children apparently healthy during the first four years of life.

Positive Wassermann Test in a Fatal Case of Estivo-Autumnal Malaria.—Guthrie McConnell, Cleveland. The Journal of the American Medical Association, 1923, vol. lxxx, p. 1123.

In this case there were no clinical findings indicative of syphilitic changes, in spite of the history of infection. The necropsy, however, disclosed very definite syphilitic lesions of the aorta, with involvement of the aortic leaflets. The experience at this hospital has been that when a necropsy has been performed on a body from a person who has given a positive blood Wassermann reaction, lesions have been discovered that were evidently syphilitic in nature. This case of malaria proved no exception to the rule.

Comparison of the Wassermann Reaction with the Sachs-Georgi Reaction and with the Sigma Reaction of Dreyer and Ward.—A. Dawson, Royal Army Medical Corps and R. O. A. Smith, Poona. Journal of the Royal Army Medical Corps, 1923, vol. xl, p. 128.

The Dreyer-Ward Sigma Test is very accurate and as reliable as the Wassermann test in the diagnosis of syphilis. The Dreyer-Ward test compares unfavorably with the Wassermann test in the time taken to put up the test. Eighty to 100 Wassermann tests can be put up in one hour, including the dilutions of reagents and testing of the complement, while it takes about an hour to put up 16 Sigma tests. The Wassermann test is extremely easily read; the authors read eight degrees of hemolysis in each of the two tubes and find it much simpler to select these figures than to pick out the degrees of flocculation in the Dreyer-Ward test. They find it very fatiguing to read a number of Dreyer-Ward tests, whereas large numbers of Wassermann tests can be read without any fatigue. In a laboratory where small numbers of test have to be made, the advantage of the Wassermann reaction does not appear to be so great, but, where large numbers have to be done and the technic is standardized, the Wassermann reaction can be done very rapidly. The sera tested came from all parts of India and Burma, many having been four to eight days in transit, but this, even in the hot weather, did not seem to affect the reaction. They have tested very septic sera and badly hemolyzed sera, and have obtained readings agreeing with clinical findings; such sera would have been useless for the Wassermann test. The Dreyer-Ward test does not necessitate the keeping of guinea-pigs, rabbits and sheep, and no amboceptor has to be prepared, a vivisection license is not required by the worker, who prepares his own reagents.

Neurosyphilis, Its Diagnosis and Treatment.—M. Q. Howard, Oklahoma City, Okla. Journal of the Oklahoma State Medical Association, 1923, vol. xvi, p. 84.

Five types of neurosyphilis are recognized based on the location of the lesions and a fairly constant set of symptoms ascribed to each type. The six positive tests are of more value in interpreting a cure than in making a diagnosis. As many cases respond to intravenous therapy alone that form of treatment should be used first. Arsenic appears in the spinal fluid within ten minutes after intravenous injections of neo-arsphenamine. The reaction from mercurialized serum intraspinously is not as severe as that from arsphenamized serum. Because of the reaction and the limitations of the dosage arsphenamized serum was not given. Juvenile paresis does not progress as rapidly as the adult type and responds more readily to treatment.

Cerebral Syphilis.—Nathaniel H. Brush, Santa Barbara, California. The California State Journal of Medicine, 1923, vol. xxi, p. 212.

As compared to tabes and general paresis, cerebral syphilis is an early involvement of the central nervous system. In the former the time that elapses from infection to development of symptoms is rarely less than ten years, in the latter the time is from three to five years. The onset of cerebral syphilis is often acute with headache, cranial nerve involvements, etc., and a mental reaction that is fairly characteristic. The Argyll-Robertson pupil occurs in fifty per cent to seventy-five per cent of all cases of paresis and in seventy-five per cent to eighty per cent in tabes, its presence in cerebral syphilis is sufficiently rare to make it a differential point of importance. Little value can be placed on the reflex changes. Ninety per cent of paretics have a positive Wassermann reaction in the blood and spinal fluid. Ninety per cent of tabetics have a positive Wassermann reaction in the spinal fluid, but only 75 per cent have a positive reaction in the blood. In cerebral syphilis the blood and spinal fluid may or may not be positive. The acute cases are the ones most liable to have the positive reactions. A greatly increased globulin content and a high cell count point to cerebral syphilis. Arsenical treatment with the assistance of mercury compounds is indicated.

Syringomyelia and Syphilis of the Central Nervous System, with Report of a Case of Tabes with a Syringomyelia Syndrome.—Claude Uhler, Dallas, Texas. Texas State Journal of Medicine, 1923, vol. xix, p. 17.

An attempt has been made to reveal the actual frequency of syringomyelia with syphilis of the central nervous system, dividing the cases into four groups: (1) Clinically observed cases of cerebro-spinal lues with syringomyelia syndromes leading to the suspicion of central localization of the luetic process or to a combination of two different processes; (2) a group of cases established clinically as syringomyelia bases; (3) anatomically combined syringomyelia and syphilis of the central nervous system, where combined disease had not been suspected during life; (4) those cases where syringomyelia and tabes had been diagnosed clinically and confirmed by autopsy. The developmental relationship between the two processes has been traced, with consideration of the proposed theories, that (a) the two processes may be quite independent of each other, and (b) the two processes may be genetically related. It is proposed that a tabetic syndrome may follow extension of a primary central gliosis into the posterior tracts or that gliosis and cavity formation are secondary to lues. This may follow from a central lying syphiloma, from an extension of the separate interstitial gliosis of the posterior tracts to involve the centre of the cord or, more likely, from toxic luetic agents or nutritional disorders, either from altered blood and lymph circulation or compression from meningitis or posterior tract degeneration. The possibility of making a diagnosis of combined disease during life, has been discussed. It is concluded that attention must be directed to a history of infection and the order of appearance of symptoms; to the type of motor disorders; to the nature and distribution of sensory changes (restricting the use of dissociated sensibility as a diagnostic aid); to the character and situation of trophic disorders, and of pupillary phenomena, particularly the significance of the Argyle-Robertson pupil.

Experimental Studies with Mercurials in Experimental Syphilis with a Brief Note on Their Clinical Application Especially as to Flumerin.—Justina H. Hill, M.S., and Hugh H. Young, M.D., Baltimore, Md. The Journal American Medical Association, 1923, vol. lxxx, p. 1365.

The marked antisyphilitic action of flumerin has been demonstrated further, fifteen doses of 5 mg. per kilogram being employed. The slight action of mercuric cyanid, given in twenty-one doses of 0.2 mg. per kilogram, and the lack of therapeutic action of mercuric salicylate, during the first part of treatment with twelve doses of 0.6⅔ mg. per kilogram, under which all animals grew markedly worse before enough mercury was absorbed to check the infection, have been shown. The slow but complete resolution of lesions under treatment with red mercuric iodid given in twenty-five doses of from 0.1⅓ to 0.2⅔ mg. per kilogram has indicated the antisyphilitic action of this drug, although the permanence of its action has not yet been demonstrated.

The Pathogenesis of Mercurial Stomatitis.—Daniel H. Bessesen, Minneapolis, Minn. Archives of Dermatology and Syphilology, 1923, vol. vii, p. 332.

The nine principal theories of the action of mercury on the body are briefly summarized. The essential literature of the pathology of mercury poisoning is analyzed under the system of organs affected, in order to see whether the known facts indicate any general underlying effects which might be involved in local lesions, such as those that occur in the mouth. From the foregoing analysis, it is evident that there are distinct indications of blood and circulatory changes which must be taken into consideration in discussing any local lesion. The results of examining a large number of sections from tissue taken from cats and ferrets, with mercury lesions are recorded. These results and their interpretations are fully in harmony with those deducted from an extensive review of the literature. In connection with the pathogenesis of mercurial stomatitis, the author believes that the general systemic action is answerable for the lesions in the same degree as the local changes.

Jaundice in Syphilitic Persons Receiving Arsenical Medication.—Louis Chargin, and Samuel Z. Orgel, New York. Archives of Dermatology and Syphilology, 1923, vol. vii, p. 495.

A moderate percentage of syphilitic patients appear to have a predisposition to the development of icterus (damaged liver). In this group the administration of arsphenamin or of its analogues causes an increase of bilirubin in the blood. It is possible by means of the tests outlined to detect a rise in the bilirubin content in the blood and therefore of a tendency to jaundice. An increase of bilirubin in the blood is a danger signal of a possible oncoming jaundice. These tests serve as a guide to safeguard patients receiving medication with arsenical preparations from the development of jaundice.

Biologic Reactions of Arsphenamin.—Jean Oliver and Ethel Douglas, San Francisco. Archives of Dermatology and Syphilology, 1923, vol. vii, p. 573.

Arsphenamin produces incoagulability of the blood both in vitro and in vivo. The action of the arsphenamin is chiefly on the fibrinogen (globulins), rendering it incoagulable to heat or thrombin. No action on thrombin could be demonstrated. Although this disturbance in the properties of the globulins is similar in nature to that caused by alkali, the action of the latter alone will not explain the results obtained in the author's experiments with arsphenamin solution.

Quantitative Studies with Arsphenamine.—A. C. Kolls and J. B. Youmans, Baltimore. Bulletin of The Johns Hopkins Hospital, 1923, vol. xxxiv, p. 149.

Although the diazo reaction employed by the authors is not given by substances normally occurring in the body fluids, at least under the conditions is which they employ the test, and is readily given by arsphenamine neoarsphenamine and the silver sodium preparation, it is also of importance to know what decomposition products of these drugs also react. During the course of the work it was noted that old solutions, which in certain instances had been made several weeks before, gave reactions with very little less intensity than fresh arsphenamine. It is well known that such solutions undergo change with the formation of less radicles. By actual determination it was shown that oxy-amino-phenyl-arsenoxide gave the test as readily as the mother substance. This compound has long been reputed to be the first oxidation product. Table 2 is a summary of the results obtained in an animal experiment in which the blood, cerebrospinal fluid, urine, and the various organs were analyzed by the method just described. The animal received disodium arsphenamine in a dosage of 20 mgm. per kilo. The results are presented as illustrative of the application of this method to experimental work.

Some Reactions in the Treatment of Syphilis and Their Probable Significances.—S. G. Gill, Norfolk, Va. Virginia Medical Monthly, 1923, vol. 1, p. 71.

In the author's series of cases, arsphenamin, and neoarsphenamin are both useful in the treatment of syphilis, but the former is more potent and should be used whenever practicable. A great many useless, unnecessary reactions from the administration of the drugs can be eliminated, thereby increasing its usefulness. There are very often many diseases and conditions associated with syphilis that we must not expect to respond to luetic treatment. Although in the author's series the severe reactions were followed by negative tests and eventually clinical improvement, they hope some day to be able to increase the tolerance of the drug to the desirous therapeutic effects without these distressing therapeutic phenomena.

Lumbar Puncture in the Routine Treatment of Syphilis.—Warren T. Vaughan, Richmond, Va. Virginia Medical Monthly, 1923, vol. 1, p. 75.

A negative blood Wassermann does not rule out central nervous system syphilis, even in those cases who have had no anti-luetic treatment. In case of doubt, a diagnostic lumbar puncture will give valuable information. The intrathecal pressure should be roughly estimated, cell count and globulin content should be recorded and Wassermann reaction should be determined. The colloidal gold reaction as a control for the Wassermann is useful. It is important to use amounts of fluid up to 2 c.c., in the Wassermann test, so that a weak positive will not be overlooked. No case of syphilis can be said to be successfully protected against late neurosyphilis until the spinal fluid has been studied and found to be normal. Early treatment of neurosyphilitic lesions, before the development of localizing signs, offers the only promise, at present, of satisfactory therapy. Spinal fluid examination affords the only means of recognizing this early involvement. Every syphilitic should have at least one lumbar puncture performed, early in the course of his disease.

The Value of Bismuth Salts in the Treatment of Syphilis.—Pardo-Castello, Havana, Cuba. Archives of Dermatology and Syphilology, 1923, vol. vii, p. 586.

The bismuth salts have marked antisyphilitic properties. Quinin bismuth iodid seems to be the compound of choice. The author has not observed a single accident with its use in over 180 injections. Sodium and potassium tartrobismuthate is painful, and stomatitis is likely to occur with its use. Spirochetes disappear from the chancre and mucous patches after the second or third injection of quinin bismuth iodid. The primary lesion and all the secondary manifestations heal in a short time, and the general disturbance and headache also disappear after the fourth or sixth injection. Tertiary lesions respond more slowly, but they finally disappear entirely. The effect on the Wassermann test is marked. It became negative in seven of nine cases. Bismuth is entitled to a prominent place among antisyphilitic remedies. Further experiments will show its real value as compared with the arsenicals and mercurials. Time alone will demonstrate whether bismuth will take the place of the other antisyphilitics or be used in combination with them. It will also show whether the effects are permanent.

Value of Treatment in General Paresis.—H. C. Solomon, Boston. The Boston Medical and Surgical Journal, 1923, vol. clxxxviii, p. 635.

General paresis is an active spirochetal disorder which can be theoretically arrested. There is considerable evidence that antiluetic treatment long continued and intensively given will arrest the paretic process in a reasonable percentage of cases especially if begun early in the disease. The author's experience has been that antisyphilitic treatment is of considerable value in the case of general paresis and that many paretics, even after the onset of marked psychotic symptoms, may recover sufficiently to return to their former occupations for a period of years, in some cases in his experience for more than seven years without a return of symptoms. Remissions may result from the use of intensive intraspinal or intraventricular injections when these apparently could not be obtained from intensive intravenous treatment alone. More potent anti-syphilitic drugs and more efficient methods of penetration of the drug into the tissues of the central nervous system may be expected to give better results in cases of general paresis.

The Therapeutic Action of Bismuth in Syphilis.—C. Levaditi, Paris. The Lancet, 1923, vol. cciv, p. 639.

Sodium and potassium tartro-bismuthate and metallic bismuth achieve rapid cicatrization of syphilitic lesions at all stages of the disease. Although bismuth has only been recently employed the author believes that, when used early and in sufficient quantity, it will cure syphilis. The absence of recurrences of the disease, and the effect on the Wassermann reaction, only serve to confirm this opinion. Equal, from a therapeutic point of view, to arsenical preparations, better than mercurial preparations, bismuth (trepol and neotrepol) is a valuable antisyphilitic remedy, particularly in those manifestations of the disease which resist the action of arsenic and mercury.

General Paresis: What It is and Its Therapeutic Possibilities.—H. C. Solomon, Boston, Mass. The American Journal of Psychiatry, 1923, vol. ii, p. 623.

General paresis is a condition which shows varying degrees of brain pathology. The process involves the meninges, blood vessels, glia and nerve cells of the cerebrum (and the spinal cord as well). It includes inflammatory and degenerative changes. There are great variations in different cases as to the amount of reaction affecting these several tissues. It is difficult anatomically to differentiate in some instances between the malignant paretic changes and the less malignant tertiary syphilitic changes, and the two may be present in the same brain. Clinically, and serologically, it is often entirely impossible to differentiate between the paretic and nonparetic forms of neurosyphilis. The therapeutic test, although of some practical applicability, is theoretically untenable, and in practice often leads to erroneous conclusions. The problem of treatment of general paresis offers a certain amount of difficulty due to the lack of any sufficiently powerful spirocheticidal drug. That this is so is seen in the consideration of cases of syphilis affecting organs other than the central nervous system. It is by no means uncommon to find mucous membrane lesions occurring in patients who are receiving arsphenamin and mercury. These lesions occur during the administration of the drug and at times are resistant to any form of therapy. Spirochetes in great numbers may be demonstrated in such lesions and are apparently immune to the drug. A similar condition undoubtedly occurs when the spirochetes are located in the central nervous system where even a smaller amount of drug can reach them. There are cases of syphilitic meningitis which do not react favorably to anti-syphilitic remedies. Here the difficulty is not explained by structure of blood supply and the tissue involved, but rather that our drugs or methods of applying them are inadeqate. We must admit that from the practical standpoint the problem is more difficult in cases of paresis than in certain other forms of neurosyphilis.

This means that we must use methods at our command more intensively than is necessary in certain other forms of syphilis. The conventional routine treatment of early syphilis namely, a half-dozen injections of arsphenamine weekly, followed by twelve or fifteen injections of mercury at a like interval, is rarely if ever of any benefit to the paretic. If one is to obtain results, the treatment must be pushed to the limit of the patient's tolerance. If depending upon the systemic treatment, arsphenamin must be given at frequent intervals over a considerable period of time. When this does not produce satisfactory results, other methods must be relied upon. For this purpose intrathecal injections have some value, but as pointed out, the injection of serum into the lumbar region is theoretically and practically inefficient as compared to cisternal or ventricular injections, because it does not reach the cerebrum in any considerable amount. Therefore, they have adopted the procedure of combining the methods of intrathecal therapy and intravenous therapy and spinal drainage, and treated the patients somewhat as follows: Semi-weekly injections of arsphenamine associated with spinal drainage, lumbar, cisternal, and ventricular injections of serum given at intervals of three or four days, and repeated for a number of months. The results obtained by this procedure have been somewhat more satisfactory than when less vigorous treatment was given. It would be logical to add to this methods which apparently have had some therapeutic benefit by increasing the immunity reaction of the patient, such as the tuberculin or sodium nucleinate injections.

Pontobulbar Crisis Associated with Sialorrhoea in Syphilis of the Nervous System.—Ernest P. Boas & Walter M. Kraus, New York. The Journal of Neurology and Psychopathology, 1923, vol. iii, p. 329.

Crises occur in patients with syphilis of the nervous system who do not present the picture of tabes dorsalis. A group of signs and symptoms due to disease of the pons and medulla or their nerves occurs in such cases of syphilis of the nervous system, and includes: (a) A profuse secretion of thin and watery saliva; (b) Gastric hypersecretion; (c) Attacks of vomiting related to salivation; (d) Tachycardia; (e) Attacks of high blood-pressure; (f) A sensation of bad taste in the mouth; (g) Pain in the suprasternal notch radiating downward to the left; (h) Diminution of pharyngeal and absence of laryngeal reflexes; (i) Disorders of sensation in the trigeminal distribution.

Studies on the Cerebrospinal Fluid with an Acetic Anhydride-Sulphuric Acid Test.—Oswald H. Boltz, N. Y. C. The State Hospital Quarterly, 1923. Vol. viii, p. 198.

The acetic anhydride-sulphuric test is 100 per cent positive with spinal fluids from cases of general paresis. Among psychiatric cases, the acetic anhydride-sulphuric test was found positive predominately in cases with neurosyphilis. The more advanced and active we find the syphilitic condition of the central nervous system, the more positive will be the acetic anhydride-sulphuric reaction. In syphilitic clinics, the test may prove to be valuable in the prognosis of neurosyphilis, in psychoses not due to or complicated with syphilis, and of a functional nature, the acetic anhydride-sulphuric test is negative. For the present the author is not fully convinced that the acetic anhydride-sulphuric test is specific for neurosyphilis, but is more apt to be evidence of the destructiveness of the Spirochaeta pallidum on nervous tissue, more an index of degenerate nerve tissue. The acetic anhydride-sulphuric test differentiates two groups of tabetics, one giving a negative reaction, the other showing a slightly positive reaction. In four cases of neurosyphilis with a negative spinal fluid Wassermann, the acetic anhydride-sulphuric test was positive.

The Relation Between Syphilis and Diabetes Mellitus.—James H. Smith, Richmond, Va. Virginia Medical Monthly, 1923, vol. xlix, p. 662.

Syphilis is an infrequent cause of diabetes mellitus. When the two occur in the same patient, antisyphilitic treatment does not often improve carbohydrate tolerance. A positive Wassermann reaction is not in itself diagnostic of syphilis in a diabetic of severe grade.

Quantitative Studies in Syphilis from a Clinical and Biologic Point of View.—John A. Fordyce; Isadore Rosen and C. N. Myers, New York. Archives of Internal Medicine, 1923, vol. xxxi, p. 739.

As a result of the examination of the blood, urine, hair and milk from about 200 subjects the authors state that arsenic is found "normally" in a large number of persons, depending on the character of their food, drink, medication and environment. It is absent in persons on a diet restricted in the amount of sweets, vegetables, meat, etc., and it is present in varying amounts in persons applying remedies containing ingredients contaminated with arsenic to inflamed or ulcerating skin surfaces, and to a greater extent in persons receiving arsenic either by mouth or intravenously or connected with the arsenicals in a preparative way. "Normal" is interpreted as meaning the result found when a large number of persons are examined. Tables given show that it is not necessary for every person to show a positive test at all times. These tables show to some extent that all drugs and foods are contributing factors in the detection of arsenic in human beings, depending, of course, on the method of manufacture and the preparation of the food. Arsenic is also secreted in the milk and is found in hair and skin tissue. It was difficult to obtain specimens from a large number of normal persons in whom they could control absolutely the character of their diet. In the few who could be relied on the analyses showed quite definitely the absence of the drug where an arsenic-free diet had been carried out. Most of their specimens were from patients with the various common skin diseases such as eczema, urticaria, psoriasis, acne, etc. In some of these patients disordered metabolism is a contributing factor and a possible cause for the variations in the amounts of arsenic found. Consideration of the results in the tables shows that a complete history of the subject is necessary before arriving at a decision regarding the arsenic content of the urine, blood or even of the organs. In the determination of the amount found ''normally'' in the body fluids the ideal way would be to hospitalize the subject in order to regulate the nature and amount of food ingested and to check up false statements regarding medication. Consideration of the ''normal'' arsenic is necessary from a medicolegal point of view. This investigation shows that it may be a constituent of the body under the conditions studied and that excessive amounts should always be considered with suspicion in patients who present themselves for examination and medication.

Extra-Genital Chancres.—Homer G. Collins, Topeka. The Journal of the Kansas Medical Society, 1923, vol. xxiii, p. 22.

Extragenital chancres are by no means uncommon and physicians, especially in the discharge of their duties, when handling known syphilitic patients, should use every precaution to prevent becoming infected. Any sore accompanied by induration and adenopathy, regardless of location, which has failed to respond to local treatments should be given the benefit of a dark-field examination.

Reinfection in Syphilis.—Captain Charles E. Brenn, Medical Corps, United States Army. The Military Surgeon, 1922, vol. li, p. 250.

When a patient known to have been a syphilitic develops a new lesion which appears to be a primary sore, the possibilities to be considered are (a) reinfection, (b) superinfection, (c) autoinfection, (d) infection with a new strain of spirochete, and (e) chancre redux. There are still many venereologists who insist that reinfection is impossible.

Syphilis in General Practice.—A. A. McLaurin, Pierre, S. D. The Journal-Lancet, 1922, vol. xlii, p. 505.

The Treponema pallida has invaded the lymph and blood streams before the primary lesion develops. Any lesion of the external genitalia, regardless of its appearance or duration, should be considered syphilitic until proven otherwise. Caustic applied to these lesions delays the diagnosis and exposes the patient to unnecessary danger.

Syphilis in Children.—H. Boyd Graham, Melbourne. The Medical Journal of Australia, 1922, vol. i, p. 265.

Deep subcutaneous injection of novarsenobillon is regarded as a simple method of treatment generally applicable for all syphilitic children. The serious sequelae are the abscesses. Larger doses of novarsenobillon than are usually recommended have been given without untoward result. The general health of the children and active lesions have been beneficially affected by this method of using novarsenobillon. Percutaneous intravenous injections are preferable in selected cases.

The Effect of Arsphenamine Treatment on Cardiovascular Syphilis in Negroes.—Moise D. Levy, Houston, Texas. Texas State Journal of Medicine, 1923, vol. xviii, p. 509.

A brief review of the literature on the use of arsphenamine in cardiovascular syphilis shows that the drug is decidedly dangerous, and that if used at all it should be employed in very small does. A series of 19 cases of cardiovascular syphilis in negroes is presented—6 cases of aneurism, 7 cases of aortitis and myocarditis, and 6 cases of aortic insufficiency. Of this series, 6 patients died, 5 showed no improvement, 1 became decidedly worse under treatment, and 7 showed a slight improvement in symptoms. It would appear from this brief study that arsphenamine is not without considerable danger in luetic cardiovascular infections in negroes, its results so far as cure is concerned being almost nil.

A Specific Sore Throat Which Passed as an Ordinary Pharyngitis and Tonsillitis, Treatment Administered for Same, with no Relief.—David B. Medalia, Boston. The Boston Medical and Surgical Journal, 1922, vol. clxxxvii, p. 637.

One must always guard against specific sore throats, though the patient gives a negative luetic history. It is important to take a blood test in cases of persisting sore throats accompanied by ulcerations, and which do not clear up under ordinary treatments.

The Diagnosis of Syphilitic Aortitis.—Wm. H. Deaderick, Hot Springs, Ark. The Journal of the Arkansas Medical Society, 1922, vol. xix, p. 109.

The number of cases in the series on which this paper is based was 28, of which 21 were aortitis alone, three of aortitis with aneurysm, and four of aortitis with aortic regurgitation. Each of the 28 cases gave a history of syphilis. In nine cases the Wassermann reaction on the blood was negative at the time of examination. In eight of these nine cases there was definite history of infection and of specific treatment. The other case gave no history of infection or of treatment, but sluggish knee jerks, irregular pupils and a positive spinal fluid Wassermann were found at the examination. The percentage of positive Wassermanns would have been higher but for recent vigorous treatment in several of the negative cases. Analyzed with reference to the outstanding symptom, that is the chief complaint, this was circulatory in only four cases and extracirculatory in fourteen. In the entire series of 28 cases, pain, including precordial or substernal distress, was the most frequent symptom, being complained of by fourteen patients, eight with aortitis alone, three with aortitis and aneurysm and three with aortitis and regurgitation. Dyspnea was elicited in the histories of ten patients, five with aortitis alone, two with aortitis and aneurysm and three with aortitis and regurgitation. Palpitation was one of the complaints of six patients, five with aortitis alone and one with aortitis and aneurysm. In the 21 cases of aortitis alone the most important physical findings were as follows: An aortic systolic murmur transmitted up, in ten cases; an aortic systolic murmur not transmitted, in three cases; impurity of the aortic first sound, in three cases; metallic aortic second sound, in nine cases. The average systolic pressure in the 21 cases of aortitis alone was 140, the diastolic 89. There were four cases presenting systolic pressures of 160 or over; 160, 160, 165 and 175 in patients aged 36, 63, 65 and 60 respectively.

The Kahn Precipitation Test for Syphilis.—William Levin, Topeka, Kansas. The Journal of the Kansas Medical Society, 1923, vol. xxii, p. 4.

A comparative study of the Wassermann test and the Kahn precipitation test was made on 258 blood specimens received in the routine work of the Public Health Laboratory. There was complete agreement in the two tests in 86.4 per cent of the specimens, relative agreement in 12.8 per cent, and complete disagreement in 0.8 per cent. The Kahn precipitation test is simple, requires few manipulations, and is remarkably accurate. It should not and probably will not replace the Wassermann test, but it should be used to check it.

Recent Studies on Spirochetes in General Paralysis.—Charles B. Dunlap, Ward's Island, N. Y. Archives of Neurology and Psychiatry, 1922, vol. viii, p. 589.

Spirochetes may be found in any part of the brain in general paralysis, but especially in the frontal parts. They are chiefly in the middle and deeper layers of the gray matter, rarely in the pia mater, almost never in the white matter, and are most often found in cases with a stormy clinical course. Spirochetes may live for many hours after the death of the patient. They strongly resist decomposition, and may change their position postmortem. Therefore, necropsy should be performed as early as possible. Spirochetes in general paralysis are either diffusely scattered or more rarely grouped in foci or swarms. They have no special relation to nerve cells or to other elements in nervous tissue, with the possible exception of blood vessels. The time at which spirochetes enter the nervous parenchyma in general paralysis, and the pathways by which they spread after entrance, are not yet determined. The spirochete of general paralysis is probably a syphilitic organism, altered biologically by various influences to which it is subjected during its long residence within its host. There is insufficient evidence that it is a special neurotropic strain different from the beginning. Experimental work with animals needs to be enlarged and well controlled. Spirochetes are not absolutely limited to the nervous parenchyma in general paralysis; although not found in the general organs of the body, they are occasionally found in the mesoblastic tissues, pia mater and in the aorta. The terms ''parenchymatous neurosyphilis'' and ''interstitial neurosyphilis'' seem hardly justifiable in the light of present studies. Spirochetes have been demonstrated in the spinal pia-arachnoid in tabes. A great field is open for further study along these lines, especially in experiments on animals. Treatment of general paralysis need not be absolutely hopeless. Some of the spirochetes, at least, are probably accessible. The modified strain of spirochete in general paralysis with its hypothetical "heightened resistance" may need to be attacked by a modified therapeutic agent different from the one that succeeds with the ordinary syphilitic strains.

The Kolmer Modification of the Wassermann Test.—J. Harper, and L. F. Curtis, United States Navy. United States Naval Medical Bulletin, 1922, vol. xvii, p. 757.

During the past six months the Kolmer technic has been used in 120 instances at the United States Naval Medical School, and from the beginning it was clearly evident that this technic was more sensitive than the complement-fixation test routinely employed (a modification of the Noguchi test, using both an acetone-insoluble lipoid antigen and a cholesterolized antigen). The Kolmer technic gives a more sensitive reaction than the older method used in the authors' laboratory. It apparently gives an earlier positive reaction in cases of primary syphilis and is much slower to become negative in cases under treatment. It apparently does not yield a false positive reaction in nonsyphilitic cases nor in cases who have had sufficient treatment. The quantitative feature enables the clinician to satisfactorily gauge the effect of antisyphilitic treatment. (A table is given which compares the results of the Kolmer technic with the Noguchi two-antigen method as employed in the authors' laboratory.)

Observations on the Colloidal Gold Reaction in Neurosyphilis.—Cecil Worster-Drought, H. J. B. Fry and G. Roche Lynch, London. The Lancet, 1922, vol. cciii, p. 1063.

A positive gold reaction in the cerebrospinal fluid is definite evidence of organic nervous disease. In syphilis of the central nervous system a positive colloidal gold reaction appears at an earlier date than the Wassermann reaction. Although dementia paralytica is usually associated with a paretic type curve and tabes dorsalis with a luetic type, definite exceptions occur; it is probable that the type of curve varies with the intensity of infection of the central nervous system rather than with the clinical type of disease. Antisyphilitic treatment on modern lines tends to modify and may even abolish a positive colloidal gold curve. Disseminated sclerosis is associated with a positive curve, the type of which varies with the intensity and stage of the disease.

Comparative Study of the Kahn and Wassermann Reactions for Syphilis.—Sobei Ide and George J. Smith, Ann Arbor, Mich. Archives of Dermatology and Syphilology, 1922, vol. vi, p. 770.

The value of the Kahn precipitation reaction is almost as great as that of the Wassermann reaction on the blood serum. This reaction is now being performed as a check on the Wassermann reaction on all serums sent to the authors' laboratory for examination. The relative ease with which this reaction can be carried out leads the authors to believe that it will attain wide usefulness in many laboratories. A point particularly in favor of the Kahn reaction is that anticomplimentary serums give no difficulty with it. Such serums are either positive or negative, depending on the presence of syphilitic reagin. While this test worked very well on the blood serum, it does not, however, work as well on the spinal fluid as does the Wassermann test. It is believed by the writers on this subject that in the very near future this drawback will be overcome by some worker who will cast light on the subject.

Experience with the Kolmer Quantitative Complement-Fixation Test for Syphilis.—Lester J. Palmer, and W. E. Gibb, Seattle. Archives of Dermatology and Syphilology, 1922, vol. vi, p. 739.

The new Kolmer quantitative complement-fixation test for syphilis differs from our old methods as follows: It shows greater sensitivity. It shows greater specificity. It gives fewer anticomplementary reactions. It is more economical. It requires somewhat more time and labor. The reactions are sharper and more easily read. It has the added value of a quantitative phase.

The Specificity of Cholesterinized Antigens in the Serologic Diagnosis of Syphilis.—Robert A. Kilduffe, Pittsburgh. Archives of Dermatology and Syphilology, 1922, vol. vi, p. 730.

Cholesterin plus reactions cannot be safely disregarded as generally nonspecific. The problem of the specificity of cholesterinized antigens should be exhaustively investigated. The occurrence of a cholesterin plus reaction constitutes strongly presumptive evidence of the presence of syphilitic reagin and necessitates a further and an exhaustive examination—clinical, historical and laboratory.

The Kolmer Modification of the Wassermann Reaction.—Robert A. Kilduffe, Pittsburgh. Archives of Dermatology and Syphilology, 1922, vol. vi, p. 709.

There are no disadvantages militating against the adoption of the Kolmer modification as a standard method of complement-fixation in the serologic diagnosis of syphilis. The method presents the following advantages in favor of its adoption, as compared to methods in common use: (a) It possesses greater delicacy. (b) It presents a greater flexibility and elasticity. (c) Strictly quantitative readings are easily made. (d) Nonspecific fixations were not obtained in this series and are, apparently, extremely rare, if they occur at all. (e) It is equally well adapted to the control of treatment as to the diagnosis of syphilis. The new antigen used in the method is superior in every way to any hitherto devised. As a means of determining the efficiency of treatment the method is far superior to any with which the author is familiar, giving fewer negative reactions than by the usual methods, and thus ensuring more protracted and adequate treatment. As far as is indicated by the evidence at hand, a positive reaction by this method constitutes extremely good presumptive evidence as to the presence of syphilitic reagin. The method is not infallible and occasionally fails to detect syphilitic reagin in known cases of syphilis, in this respect being similar to all other technics, except that such false negative reactions occur with much less frequency. Absolute reliance as to the absence of syphilitic reagin at a given time cannot be placed on the results of a single negative reaction by any method of complement fixation yet devised. In early primary syphilis the Kolmer modification gives earlier and stronger results than routine methods. The results with this method are in close agreement with the clinical findings in a high percentage of cases. It is strictly quantitative method and as such better adapted to the study of treated syphilis. It appears to be eminently worthy to supersede and supplant the methods now in common use. It presents by far the most acceptable technic yet proposed for adoption as a standard method and as such should be subjected to extensive, exhaustive and impartial trial and study.

The Wassermann Test.—David L. Belding, and Charlotte B. Adams, Boston. The Boston Medical and Surgical Journal, 1922, vol. clxxxvii, p. 815.

In 5198 routine cases in a Boston Maternity Hospital, the Wassermann test showed some degree of positivity in 9.2 per cent, was definitely positive in 7.8 and strongly positive in 4.6. Only 9.8 per cent of the positive cases gave definite clinical evidence of syphilis, although an additional 19.9 per cent showed suspicious findings. Positive Wassermann tests, with cholesterolized antigens, in pregnant women are not comparable to similar tests in nonpregnant, owing to certain blood changes, and therefore do not either represent the actual incidence of syphilis in a community or the per cent of positive tests in healthy nonpregnant women. Statistical studies from various cities cannot be accurately compared, owing to differences in technic and material. For reference all Wassermann surveys should be accompanied by a statement of the method of performing the test and a description of the status of the patient. Owing to longer exposure, the per cent of positives increased with age and length of married life. The high incidence of syphilis in the negro, twice that in the white race, necessitates the exclusion of this race, in certain statistical comparisons. The prevalence of syphilis varies with different nationalities. The per cent of positives increases inversely as the wealth of the patient, and also differs according to occupation.

The Colloidal Benzoin Reaction in the Cerebrospinal Fluid.—J. Henry Dible, Glasgow. The Lancet, 1922, vol. ccii, p. 1090.

The negative reaction occurs with normal cerebrospinal fluid. The positive reaction indicates an alteration in the cerebrospinal fluid which is very probably syphilitic in nature. An ambiguous reaction indicates a pathologic condition in the cerebrospinal fluid, but does not indicate its exact nature.

Continuation of a Report Made on a Comparison of the Sigma and Wassermann Reactions.—Lieutenant-Colonel H. Marrian Perry, and Major E. C. Lambkin, Royal Army Medical Corps. Journal of the Royal Army Medical Corps, 1922, vol. xxxviii, p. 440.

In a series of 486 cases the results of both tests were in agreement in 479, while in 7 cases discordant results were observed. Of these cases, 3 exhibited a positive Wassermann reaction, but yielded negative results on application of the Sigma test, while 4 were positive by the Sigma test but returned as negative by the Wassermann reaction.

A Comparison of the Colloid Flocculation Test (Dreyer-Ward Technic) with the Wassermann Reaction for the Diagnosis of Syphilitic Infection.—H. J. B. Fry, London. The Journal of State Medicine, 1922, vol. xxx, p. 396.

The colloid flocculation test (Dreyer-Ward technic) is a rapid, simple, and efficient test for routine laboratory diagnosis. The colloid flocculation test is as sensitive as the Wassermann reaction in the case of sera, but is slightly less sensitive than the Wassermann reaction in the case of cerebrospinal fluids. The sensitiveness of the test is appreciably increased by incubation to twenty-four hours. False positive reactions from prolongation of the incubation period have not been a source of error. The clinical evidence is at present insufficient to determine whether the Wassermann reaction or the flocculation test is the better measure of the effect of treatment.

Influence of Saturation on Properties of Antigen in the Wassermann Test.—Carl L. A. Schmidt and S. E. Coffee, Berkeley, Cal. The Journal of Infectious Diseases, 1923, vol. xxxii, p. 119.

Saturation of the lipoid commonly used as the antigen in the Wassermann test for syphilis was accomplished with the aid of hydrogen and colloidal palladium according to the method described by Paal. Both the unsaturated and the hydrogenated lipoid preparations are capable of acting as antigens in the Wassermann reaction. The hydrogenated lipoid preparation is distinctly more antialexic (anticomplementary) than the untreated antigen.

Wassermann and Flocculation Tests.—A. L. Urquhart, London. The Lancet, 1923, vol. cciv, p. 125.

That the flocculation test gives as reliable results as the Wassermann reaction. That the flocculation test is preferable to the Wassermann reaction on account of its greater simplicity. That sheep's heart extracts make satisfactory antigens, and that similarity of antigenic property may be obtained by adjustment of the amount of cholesterol added to the heart extract. That contamination or hemolysis in the sera may give rise to false positive readings and such sera should not be used in the test. That the presence of bile, pigment, or an anticomplementary state of the serum does not interfere with the flocculation test.

The Status of the Negative Wassermann Reaction.—Robert A. Kilduffe, Pittsburgh. The Journal of the American Medical Association, 1922, vol. lxxix, p. 2215.

A negative Wassermann reaction is of value only when intelligently interpreted in conjunction with the other findings; a single negative reaction is of little value in the presence of suggestive clinical findings; and as evidence of cure, a single negative reaction is worthless.

Studies of the Formol and Wassermann Reactions.—Manuel Armangue and Pedro Gonzales, Barcelona, Spain. The Journal of Infectious Diseases, 1922, vol. xxx, p. 443.

A table is given of the results of the Wassermann and formol reactions in 174 serums of suspicious cases. They obtained positive formol reactions in 67 per cent of cases of malignant tumors which gave negative Wassermann reactions. They have, therefore, a higher percentage of positive reactions among patients with malignant tumors than among syphilitic patients. The serum of a woman, taken 8 days after the extirpation of a sarcoma of the neck, reacted only moderately. They were unable to obtain serum of this case subsequently. The serums of pregnant women (7 to 9 months) always gave a negative formol reaction. Serums of normal dogs, rabbits, guinea-pigs, hogs, etc., were always negative, but often positive in pathologic conditions. In cases of dogs, 28 per cent positive reactions were obtained, and this was practically constant in tenia infestations. In rabbits affected with coccidiosis of the peritoneal cavity, 34 per cent gave a positive reaction, while 100 per cent positive reactions were obtained if the spleen harbored coccidia or other parasites. A rabbit with hydatid cysts also gave a positive reaction.

Wassermann Variations.—Lester J. Palmer, Seattle. The Journal of the American Medical Association, 1922, vol. lxxix, p. 724.

A safe and efficient standardized technic should be adopted and required of all laboratories. A higher degree of efficiency should be demanded of technicians. Laboratories performing the Wassermann test should be authorized and supervised by medical state or federal authority. The profession at large should have a better understanding of the technical difficulties of the Wassermann test and of its value as a diagnostic procedure.

The Reliability of the Sachs-Georgi Test for Syphilis.—John W. Rice, New York City. The Journal of Infectious Diseases, 1922, vol. xxxi, p. 444.

When roughly classified into ''positive'' and ''negative'' the Sachs-Georgi tests agreed with the Wassermann tests in 94.4 per cent of 1,000 cases tested. The Sachs-Georgi test appears to be less sensitive than the Wassermann reaction in patients receiving antisyphilitic treatment and in cases of cerebrospinal syphilis. The Sachs-Georgi test is just as sensitive as the Wassermann test in untreated cases of primary, secondary and tertiary syphilis. The specificity of the Wassermann alcoholic antigen under the four-hour ice box treatment can be questioned when the presence of bile salts in the patient's serum is ignored. With this unknown quantity controlled, the Sachs-Georgi test would show a still more favorable comparison with the Wassermann reaction as a routine test. In four cases in which the patient's serum was anticomplementary in the Wassermann test, the Sachs-Georgi test gave a definite and reliable diagnosis in each case. Because of the simplicity and reliability of the test, as shown by the data presented, the Sachs-Georgi test should attain a range of usefulness in the diagnosis of syphilis far in excess of that accredited to it at the present time.

Relative Value of Sachs-Georgi and Wassermann Reactions in Diagnosis of Syphilis.—Charles F. Craig and William C. Williams, Washington, D. C. The Journal of the American Medical Association, 1922, vol. lxxix, p. 1597.

The results of parallel Sachs-Georgi and Wassermann reactions on 1,748 specimens of blood serum from as many individuals gave a total agreement in results of 85.5 per cent. The disagreements, however, were most serious, no less than 33.3 per cent of the positive Wassermann reactions being missed by the Sachs-Georgi test in known infections with syphilis, while 26.5 per cent of the positive Sachs-Georgi reactions were not confirmed by the Wassermann test nor by clinical findings. These disagreements in tests performed under ideal conditions for comparison, by two separate investigators, were so radical in character and so important from a diagnostic standpoint, that the authors do not believe that the Sachs-Georgi reaction alone should be relied on as a diagnostic method for syphilis under any conditions. The difficulty of reading slight Sachs-Georgi reactions and differentiating them from precipitation due to other causes in the serum tested is so great, in many instances, that no reliable conclusion can be reached, thus leaving the test open to so much individual interpretation that it destroys the scientific value of the results. The widely divergent results with the test reported in the literature are conclusive proof of this statement. The Sachs-Georgi test, using the technic recommended by the originators, or slight modifications of this technic, is an interesting reaction from a theoretical and speculative standpoint; but it is greatly inferior, in its practical application to the diagnosis of syphilis, to the Wassermann test or any of its accepted modifications. The Sachs-Georgi test should never be used to the exclusion of the Wassermann test in the diagnosis of syphilis, and a positive result with the Sachs-Georgi test should always be checked up by a Wassermann test.

Studies on Blood Cholesterol in Syphilis.—Albert R McFarland, Rochester, Minn. Archives of Dermatology and Syphilology, 1922, vol. vi, p. 39.

The positive Wassermann reaction on the blood apparently does not depend on high cholesterol value. While it is interesting to corroborate this fact, it is not surprising in view of the probable complexity of the Wassermann reaction. Blood cholesterol values in syphilitic patients, in general, tend to be medium and low rather than high. The occasional high values might possibly be explained on some other basis, but no attempt was made to determine this, since the study was confined to syphilis. This may mean that cholesterol as an agent of defense is low in a chronic disease like syphilis, just as leukocytosis is low in chronic infections; but from a practical standpoint it cannot be said that the cholesterol determinations, with the possible exception of findings in the cases of involvement of the central nervous system, have afforded results much different from those to be expected from a similar series of nonsyphilitic patients. The amount of arsphenamine given and the time between injections do not obviously affect the blood cholesterol values. If cholesterol is an agent of defense in syphilis, it has not been detected in most cases in greater amount than might be expected in a series of average nonsyphilitic persons, and hence it is not affected materially by treatment for syphilis. The majority of syphilitic patients have high or normal differences between the Blood I and Blood II values, while only a few have low differences; the significance of this has not been determined. There is, apparently, no relation between the cholesterol value and the clinical and serologic response of the patient. The only recognizable relation between the clinical type of syphilis and blood cholesterol values is the large proportion of high cholesterol estimations in syphilis of the central nervous system.

The Kahn Test for Syphilis in the Public Health Laboratory.—C. C. Young, Lansing, Mich. American Journal of Public Health, 1923, vol. xii, p. 96.

The laboratory diagnosis of syphilis based on the combined results of the Wassermann and Kahn tests possesses a higher degree of accuracy than that of the Wassermann test alone. The clinical application of the Kahn test both in the diagnosis and treatment of syphilis compares favorably with the Wassermann reaction. The simplicity of the procedure of the Kahn test makes it readily applicable as a routine procedure in a public health laboratory. The employment of the Kahn test as a check on the Wassermann test will help reduce the element of skepticism associated with the older test.

Marked Atrophy in Early Tabes.—Herbert Leighton Fossey, Philadelphia. New York Medical Journal and Medical Record, 1922, vol. cxvi, p. 282.

The patient, a young white man, thirty years of age, was admitted into the Philadelphia General Hospital, August 23, 1921, complaining of gastric pains, vomiting and urinary incontinence. The patient appeared to be very sick. Physical examination revealed a severe form of cystitis, pyelitis and infected penis due to continuous friction of the urinal. He was suffering intensely from the pains of gastric crises and persistent vomiting which had been present for the past six weeks. Two weeks prior to entering the hospital he had been operated upon for appendicitis, but with no relief from the symptoms. He presented the typical syndrome of tabes dorsalis. Four plus Wassermann in all antigens in the spinal fluid and a typical luetic colloidal gold curve.

The most striking objective finding in the case was the extreme atrophy in so young a patient and at so early a stage of the disease. The disease was of four years' duration and the symptoms started one year after the initial lesion. He had never been sick before, had been in the Navy, and had been a large boned, well developed, strong, healthy young man.

Some Remarks on Tests for Cure of Syphilis.—Major Guy L. Qualls and Captain Alberto G. de Quevedo, Medical Corps, United States Army. The Military Surgeon, 1923, vol. lii, p. 140.

In this series thirty-nine tests for cure have been performed, twenty-nine cases are native Porto Ricans and ten on soldiers born in the United States and contracting syphilis there. In the Porto Rican troops the percentage of ''Cures'' is 96.6 per cent, and in the American troops the percentage is 66.6 per cent. It is highly probable in the cases of Porto Ricans, that they were in most instances infected with an organism of low virulence, slight invasive or localizing power or that they are relatively immune. It would not be logical to predict the disappearance of syphilis in man, however; if all cases could be treated to cure, it would be easy to imagine it as a rare disease among the more civilized nations in the course of three or four generations. A negative provocative blood Wassermann should never be accepted as a cure. Many cases of active destructive lesions of the central nervous system may exist and the provocative Wassermann be persistently negative. In that two cases were not observed for one year after treatment was discontinued, tests for cure, however, are considered negative, the question arises: Could not cure in many cases be determined before the lapse of one year? Only future work can determine this question. Tests for cure should be given in all cases with a positive history of syphilis in which marriage is contemplated, and, if not found free from syphilis, marriage should be delayed until cured. Tests for cure should be performed upon all soldiers with a positive record of syphilis in which the infection has become latent, the patient notified of his condition and referred for treatment if found positive. Only by this system of follow up or a similar one can it be determined whether the neurosyphilitic is ever cured or whether certain forms of the latent neurosyphilide of today becomes the paretic or the tabetic in the future.

Tumor Formation after Injection of Mercuric Salicylate in Vegetable Oil.—Irwin C. Sutton, Anaheim, Calif. Archives of Dermatology and Syphilology, 1923, vol. vii, p. 223.

Owing to asepsis and the selection of the less irritating mercury salts, nodosities following the deep injections of mercury are rather rare. When they do occur they are due to: (1) the use of mineral oil as a vehicle for the salt; (2) reaction from the presence of the mercury, or (3) traumatic gummas. By far the greatest number of nodular lesions at the site of puncture are due to the use of mineral oil as a vehicle for the mercury. In spite of the wide publicity that has been given the dangers from its use, liquid petrolatum still enjoys a dubious popularity. When severe local reactions follow the intramuscular injection of mercury in vegetable oil, it is conceivable that the element itself is at fault, or that the resulting lesions are expressions of allergy and are, therefore, traumatic gummas. The nature of the reaction can be ascertained from the clinical picture and from examination of the oil, and by an early roentgen-ray examination and by biopsy.

Results in the Treatment of Wassermann-Fast Syphilis by Intravenous Mercuric Chlorid.—A. H. Conrad, M.D., and C. H. McCann, St. Louis. Archives of Dermatology and Syphilology, 1922, vol. vi, p. 50.

Although the number of patients is at present small, the authors lead us to believe that in those cases in which the routine treatment has failed to reduce the Wassermann reaction or improve the clinical symptoms, mercury administered intravenously should be given a fair trial. Advantages claimed for this method over other modes of mercuric injections are that quicker results in treatment are obtained, a more accurate grading of dosage is made possible; the course of the disease can be more carefully observed, and a practically painless injection is assured the patient.

Mercurosal in the Treatment of Syphilis.—H. N. Cole, J. R. Driver, and J. G. Hutton, Cleveland. The Journal of the American Medical Association, 1922, vol. lxxix, p. 1821.

Among the therapeutic effects produced, the authors noted in four instances a beginning stomatitis after two or three injections, indicating certain mercurial effects from its action. Moreover, according to their records, quite a large number of their patients were much improved from its use. However, careful examination of their figures would not lead them to believe that this preparation is superior to any one of several other old, well-tried mercurials. In seven instances (approximately 20 per cent), the patients become worse following treatment with the drug; and ten of the patients, almost 25 per cent, showed no improvement. Certainly, comparison of this drug with red mercuric iodid by the injection route, and with mercurial ointment in several instances demonstrated that the latter two remedies had at least an equal, if not a superior, antisyphilitic therapeutic action. Moreover, the drug had far from the high spirocheticidal value, which the printed data of its manufacturers led the authors to expect. In those patients whom they followed with a daily dark-field examination, the spirocheticidal value of the drug was certainly not so high as that expected when using red mercuric iodid or mercurial ointment. The effect of the Wassermann reaction over a short period of time was practically nil. The drug when given intramuscularly seemed to be moderately well tolerated, but not any better than red mercuric iodid. Intravenously, however, in four of twenty-three patients, a sclerosis of the vein developed, this despite claims of the manufacturers that there was no deleterious action of the drug on the vein walls. In the twenty-three patients treated by the intravenous route, a total of 226 injections, or an average of nine for each patient was given. The total amount of drug given was 26.7 gm., or an average of 1.16 gm. of Mercurosal for each patient. According to the reports of its manufacturers, the drug contains 43.8 per cent of metallic mercury. Therefore, each one of their patients received an average of 0.508 gm. of metallic mercury by the route while under the treatment. The fifteen patients treated intramuscularly received a total of 160 injections, an average of not quite eleven injections for each patient. The total amount of drug given was 8.75 gm., or an average of 0.58 gm. of Mercurosal for each patient or 0.254 gm. of metallic mercury.

Erythema Multiforme Bullosum Caused by Arsenic. Report of a Case.—William J. McDonald, Boston. The Boston Medical and Surgical Journal, 1922, vol. clxxxvii, p. 847.

M. R., Female, aged forty years, was admitted to Carney Hospital on June 7, 1922. The patient presented an acute bullous eruption of the palmar and dorsal surfaces of the hands and fingers, and the plantar surfaces of the feet. She complained of itching and a feeling of tension and burning, but no pain. The bullae varied in size from that of a pea to the dimension of a pigeon's egg. They were very tense and, from confluence, some were multilocular. The skin, raised over the tense bullae, was pale and white. The eruption was confined to the parts mentioned. The contents of the bullae consisted of clear serum. Nine days previously, on May 30, the patient had consulted a dental surgeon. A carious tooth was treated and an arsenical preparation was inserted in the tooth for the purpose of devitalizing the nerve of supply. Two days later, on June 1, she noticed that her hands and feet were slightly swollen and were itchy. On June 5, she consulted a physician and was given Fowler's solution, four minims thrice daily, after meals. After the fourth dose she fainted, for the first time in her life. On the same day, the bullous eruption suddenly appeared. She was admitted to Carney Hospital on June 7.

Sulfarsenol in the Treatment of Syphilis.—F. Carminow Doble, Eng. The Lancet, 1923, vol. cciv, p. 70.

The disappearance of Spironema pallidum from the lesions, as shown by the dark ground examination 24 and 48 hours after an injection of this drug, compares very favorably with intravenous injections of the same dose of neosalvarsan and neokharsivan. The clinical results and the effect on the complement-fixation test of the blood equals those of any other drug. The action on the cerebrospinal fluid is not so marked as that obtained by silver-salvarsan.

Reactions Following the Intravenous Administration of Arsenobenzene Compounds.—A. Reith Fraser, Cape Town, S. Africa. South African Medical Record, 1922, vol. xx, p. 398.

Reactions may be classified as trivial and severe, or usefully, early and late or cumulative. Early side-effects again may be sub-divided into (1) those occurring during the injection, and (2) those following within 24 hours of the injection. (1) Those occurring during the injection: (a) nitritoid crisis; (b) syncope; (c) pain in the gums and teeth; (d) peculiar taste and smell. (2) Those following within twenty-four hours of the injection: (a) headache, rigor and pyrexia; (b) vomiting and diarrhea; (c) edema may be general or localized; (d) herpes labialis; (e) cutaneous disturbances; (f) coryza and hyperaemia of the conjunctivae; (g) hepatic tenderness; (h) hypersalivation; (i) aggravation of nonluetic conditions.

Arseno-Benzol in the Treatment of Syphilis.—Claude H. Mills, London. The Journal of State Medicine, 1922, vol. xxx, p. 507.

In drawing a comparison between the ''606'' and ''914'' groups of the arseno-benzol preparations as to their relative merits in the treatment of syphilis the author is firmly convinced that ''606'' is of greater therapeutic efficacy than the ''914'' products when administered in equivalent doses intravenously (Ehrlich's ratio). This is less marked in early than in later cases where the infection has progressed for three months onward in the absence of treatment. In such cases the treponemata have had ample opportunity to reach relatively avascular sheltered recesses unchecked other than by the varying and always inadequate production of antibodies. The slower elimination of the ''606'' preparations, after injection, and therefore the greater likelihood of a large proportion being converted into the spirochaeticidal derivative, is the probable explanation. In old standing, and commonly called intractable cases, the ''606'' preparations hold out a better chance of converting a positive Wassermann to a negative reaction in the blood than do the ''914'' preparations by the intravenous route.

Treatment of Arsphenamine Dermatitis and Certain Other Metallic Poisonings.—William L. McBride and Charles C. Dennie, Kansas City, Mo. Archives of Dermatology and Syphilology, 1923, vol. vii, p. 63.

Sodium thiosulphate given intravenously and by mouth rapidly shortens the course of arsenical dermatitis. It is a successful neutralizing agent for acute and chronic mercurial poisoning. To secure the best results, it must be given intravenously. In its pure form, it is nontoxic up to 2 gram doses. Certain conditions which impair the liver or kidneys are predisposing factors in the production of arsphenamine dermatitis. Certain warnings are often given which, if carefully observed and heeded, will prevent its appearance.

Contributory Factors in Postarsphenamine Dermatitis.—John H. Stokes, and Edward P. Cathcart, Rochester, Minn. Archives of Dermatology and Syphilology, 1923, vol. vii, p. 14.

It has been the authors' experience that cutaneous reactions to arsphenamine in general are not a function of the amount of the drug administered; and that they show a distinct tendency to occur early in the course of its administration, rather than late. Comparative and direct clinical analysis indicates that postarsphenamine cutaneous reactions have no clinically demonstrable connection with the administration of mercury (except as an external irritant in inunctions); neither do they seem dependent on any renal abnormality or injury detectable by the ordinary laboratory tests. In other words, they find no clinical evidence that arsenic retention due to renal injury by mercury is a cause of arsphenamine dermatitis. In a great proportion of their cases, they find evidence that chronic focal and acute prodromal or intercurrent infections form a part of the complex on which arsphenamine cutaneous reactions develop. The severity of the cutaneous reactions they have observed has stood in a rough direct relation to the extent of the infection factor. The authors have observed serious and even fatal results associated with rapid extension and generalization of a previously mild dermatitis follow the stirring up of a focus of infection. They have witnessed the immediate involution of a severe and extending dermatitis on the total extirpation of a septic focus, in one case. This favorable outcome, however, is distinctly exceptional. They submit a variety of circumstantial evidence based on studies of the prodromes, the systemic symptoms, epidemiologic considerations and fragmentary bacteriologic findings, which seem to render still more plausible the conception of infection as an important part of the causative background of the exanthematic and exfoliative syndromes complicating the administration of arsphenamine. A theory proposed of the mechanism of postarsphenamine dermatitis based on an allergic instability or idiosyncrasy produced either by colloidal changes secondary to arsphenamine injection, especially if accompanied by repeated reaction, or by chronic or sudden absorption of a bacterial sensitizing protein from a focal or acute infection, as the fundamental premise. On the allergy, the vasodilator toxic action of arsenic, the possible vasodilator effect of an acute shortage of epinephrin from arsphenamine injury to the suprarenal, or the vasodilator and irritative local effect of mercurial inunctions or iodine, or of other local applications, and perhaps all of them at once, react. The increased amounts of bacterial protein antigen or of arsenic as such, brought to these sites of vasodilation and irritation, still further excite the sensitized cells of the skin and other tissues to an acute inflammatory reaction. Injury to the liver from arsenic, from chronic or acute infection or from repeated allergic shock due to a series of injections in a patient already somewhat hypersensitive, may assist in the development of allergy, pervert the metabolism of arsenic, leaving it free in the blood or tissues, or interfere with the natural defense against the protein toxins of chronic focal or acute infections. The authors believe that their view reconciles and combines several conflicting or partial theories and a variety of seemingly incongruous clinical facts.

A Lichen Planus Eruption after Arsphenamine.—Lawrence K. McCafferty, New York. Archives of Dermatology and Syphilology, 1922, vol. vi, p. 591.

This case presented the clinical and histologic picture of lichen planus. The eruption followed shortly after the administration of arsphenamine. Cases of arsenical dermatitis closely simulating lichen planus have previously been described. In the case reported, symptoms and lesions of arsenical poisoning support the belief that arsphenamine caused this eruption.

The Effect of Antisyphilitic Treatment on the Kidney.—W. F. Lorenz and W. J. Bleckwenn, Madison, Wis. The Wisconsin Medical Journal, 1922, vol. xxi, p. 211.

All cases of syphilis before treatment should be carefully studied to determine whether or not the kidneys are functioning properly. Many cases of syphilis will be found to be suffering from nephritis of varying degree which will clear up under antisyphilitic treatment, demonstrating probably the syphilitic origin of that nephritis. These kidney function tests have the apparent advantage of disclosing kidney embarrassment before the usual signs of albumin and casts are demonstrated in the urine. The authors advocate the use of the kidney functional tests, before, during and after drug administration. If it is found that the drug administration increases the renal abnormality it then becomes a matter of selecting the least irritating of the antisyphilitic measures. In a borderline case whose renal mechanism might easily be injured by the larger doses of a drug generally employed, a careful study of the renal function will disclose the amount of drug that can be tolerated without such injury. The most important finding not observed before is that a kidney function test made immediately after drug administration cannot be accepted as evidence of kidney impairment.

A Modification in the Routine Treatment of Syphilis.—M. Sydney Thomson, London. The British Journal of Dermatology and Syphilis, 1923, vol. xxxv, p. 1.

The organic compounds of arsenic, although not possessing the specificity at one time claimed for them, are yet of undoubted value. The almost miraculously rapid disappearance of signs and symptoms in any early case, consequent on their use, must not be allowed to overshadow the essential importance of continuous mercurial administration. Nor must it be forgotten that the salvarsan group itself is not without danger to the patient. It is claimed that the method of administration here described reduces this danger to a minimum without in any way impairing the efficiency of the treatment. The rate of excretion of arsenic must be considered and its accumulation avoided if it is desired to eliminate all possibility of disaster.

Treatment of Neuro-Syphilis.—J. Grant Marthens, Dayton, O. Medical Times, 1922, vol. l, p. 45.

All cases of neurosyphilis should receive the benefits of intensive intraspinal therapy. The incidence of improvements after treatment is greater than the ordinary remissions characteristic of paresis. Paretics show a greater degree of improvement after the administration of mercurialized serum than of fortified salvarsanized serum. Mercurialized serum seems to be contraindicated in taboparetics. The use of fortified salvarsanized serum has been discontinued and in its stead 10 c.c. of .85 saline made of freshly double distilled water is used to which the required dose of salvarsan is added. The original maximum dose of .5 mg. to the fortified salvarsanized serum is now the minimum, the maximum dose being 1.5 mg. The mercurialized serum has also been discontinued. Those patients who received a series of mercurialized serum showed marked immediate and continued mental improvement but after a period of time manifested a great degree of physical impairment.

The Treatment of Neurosyphilis at the Manhattan State Hospital.—Isaac J. Furman, New York. The State Hospital Quarterly, 1922, vol. viii, p. 84.

If a case of neurosyphilis is to be treated at all, it should be done as soon as possible after admission. Every patient to be treated should be thoroughly and properly prepared before each treatment. The greatest care should be exercised in the administration of any drug, but especially, arsenic intravenously. The intravenous injections of arsenic and the intramuscular injections of mercury are attended by potential dangers that cannot be disregarded. The physical and mental condition of many patients are improved by treatment, as shown by the greater number discharged while under treatment, and by the fewer patients confined in bed. The serological findings especially the cytology and globulin, are favorably influenced by treatment, and more markedly so when the treatment is combined with spinal drainage. There seems to be some correlation between the progress of the case and the spinal fluid findings. In several cases, the fluid indicated a rapidly approaching unfavorable outcome, even before it was apparent in the patient's general condition. There is a general impression that treated cases more often die suddenly of convulsions than of long continued decline and exhaustion. It might be offered as a suggestion that the treatment causes an improvement in the meningitis and an absorption of the exudate. As a result, the patient remains mentally clearer and physically stronger, but the progress of the disease in the deeper tissues is probably not influenced to any considerable extent.

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VOL. VII

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INDEX TO VOLUME VII

AUTHORS INDEX

C

Corbitt, H. B. (*See* Myers and Corbitt), 352

Cornwall, Leon H., and Myers, C. N. A clinical and biochemical study of neurosyphilis, 287, 629

Culver, George D. (*See* Montgomery and Culver), 560, 663

Cumston, Charles Greene. Remarks on visceral syphilis, 671

D

Deaderick, Wm. H. Syphilis of the adrenals, 72

Duncam, A. G. B. (*See* Fraser and Duncam), 160

F

Fordyce, John A., Rosen, Isadore, and Myers, C. N. Quantitative studies in syphilis from a clinical and biological point of view. III. Arsenical content in scales, blood and urine in arsenical and nonarsenical eruptions, 209

—, —, and —. Quantitative studies in syphilis from a clinical and biological point of view. IV. Arsenic content in the blood at various intervals after intravenous injections of salvarsan, 225

—, —, and —. Quantitative studies in syphilis from a clinical and biological point of view. V. Arsenic content of the blood and spinal fluid after neosalvarsan in the Swift-Ellis method of treatment, 444

—, —, and —. Quantitative studies in syphilis from a clinical and biological point of view. VI. Arsenic content of the spinal fluid after salvarsan in the Swift-Ellis method of treatment, 478

—, —, and —. Quantitative studies in syphilis from a clinical and biological point of view. VII. Arsenic content of the spinal fluid after salvarsan and drainage, 513

—, —, and —. Quantitative studies in syphilis from a clinical and biological point of view. VIII. The arsenic content of the blood after intravenous injection of silver salvarsan, 528

Fox, James C., Jr., and Sanderson, Everett S. Observations on the Kahn precipitation reaction for syphilis, 687

Fraser, A. Reith. (*See* Sichel and Fraser), 665

— and Duncam, A. G. B. Reactions following arsenobenzene administration and their treatment, 160

G

Gatewood, Wesley E., and Kolodny, Anatole. Gastric and intestinal syphilis. Report of a case. Clinical course and morbid pathology, 648

Goodman, Herman. The syphilis department of the In-Patient Hospital: Its personnel, organization and equipment, 377

—. (*See* Parounagian and Goodman), 43, 563

Grinker, Julius. Diagnosis and treatment of syphilis of the nervous system, 617

Gutman, Jacob. The effects of mercury inhalation upon the animal organism, 1

—. The mercury inhalation therapy of syphilis, 145

—. Mercury inhalation therapy of syphilis—shall it be condemned? 326

—. Mercury versus arsphenamine in the treatment of syphilis, 347

H

HATA, SAHACHIRO. On the prevention of syphilis of the central nervous system, 720

HAZEN, H. H. Practical observations on syphilis, 83, 417

HINKELMAN, A. J. The fundamental principles of the Wassermann reaction, 699

HINTON, WILLIAM A. The Wassermann reaction in pregnancy, 155

HUFFER, EARL W. Venereal disease clinic, the Toledo Municipal Hospital, 56

I

IRGANG, S. Sulfarsenol in the treatment of syphilis, 318

K

KAHN, R. L. Observations on Kahn precipitation reaction for syphilis, 389

KOLODNY, ANATOLE. (*See* Gatewood and Kolodny), 648

L

LYNCH, KENNETH M. The comparative value of Kolmer's new antigen in the routine Wassermann test, 612

M

MCARTHUR, D. C. Syphilis as we see it among the natives of Bechuanaland today, 569

MONTGOMERY, DOUGLASS W., AND CULVER, GEORGE D. Chancre in the axilla, 560

— AND —. Paralysis of the seventh cranial nerve in early constitutional syphilis, 663

MYERS, C. N. (*See* Cornwall and Myers), 287, 629

—. (*See* Fordyce, Rosen and Myers), 209, 225, 444, 478, 513, 528

—. Argyria and its relation to silver therapy, 125

— AND CORBITT, H. B. Toxicity and trypanocidal activity of tartrobismuthate and its relation to the treatment of syphilis, 352

O

OELZE, F. W. A case of syphilitic chancre on the scrotum of a patient without penis, 410

P

PARÉ, AMBROISE. Epoch-making contributions to the study of syphilis, 726

PAROUNAGIAN, MIHRAN B., AND GOODMAN, HERMAN. Syphilitic genital chancre, 43

— AND —. Chancre of the lip, 563

R

REASONER, MAJOR M. A. Controlled prostitution in Coblenz, Germany, 713

ROCKWOOD, REED, AND SANFORD, ARTHUR H. The Wassermann reaction in diabetes, 679

ROSEN, ISADORE. (*See* Fordyce, Rosen and Myers), 209, 225, 444, 478, 513, 528

S

SANDERSON, EVERETT S. (*See* Fox and Sanderson), 687

SANFORD, ARTHUR H. (*See* Rockwood and Sanford), 679

SCHOENRICH, HERBERT. A case of syphilitic re-infection, 153

SICHEL, ALAN W. S., AND FRASER, A. REITH. Hemianopia as the sole clinical feature in untreated secondary syphilis, 665

SUTTON, IRWIN C. The use of sodium thiosulphate in the treatment of postarsphenamine dermatitis exfoliativa; report of a case, 608

W

WYNN, JAMES. Paresis with negative spinal fluid, 323

GENERAL INDEX

A

Abstracts, 183, 412, 736
Acquired syphilis by genital chancre in male children, with report of a case in a boy five and one-half years, 413
Adrenals, syphilis of, 72
Anticoagulating action of the arsenobenzols on blood, 749
Application of the Warthin-Starry Silver-Agar method to the demonstration of spirochaeta pallida in the spinal fluid by means of coagula obtained by the Alzheimer method, 740
Argyria and its relation to silver therapy, 125
Arsenic content in the blood at various intervals after intravenous injection of salvarsan, 225
  of the blood after silver salvarsan, 528
  of the blood and spinal fluid after neosalvarsan, 444
  of the spinal fluid after salvarsan, 478
  of the spinal fluid after salvarsan and drainage, 513
Arsenical content in the scales, blood and urine in arsenical and neoarsenical eruptions, 209
Arseno-Benzol in the treatment of syphilis, 779
Arsphenamine, 205
Arsphenamine vs. neoarsphenamine with a report of 1,609 injections, 739
Associated syphilis and tuberculosis, 415
Asthma and septicemia in syphilis, 753
Asymptomatic neurosyphilis, 201
Axillae, chancre in, 560

B

Backache, syphilitic, 415
Bacterial endocarditis as a sequel to syphilitic valve defect, 184
Biologic reactions of arsphenamine, 738, 744, 760
Bismuth in the treatment of syphilis, 739, 745
  Report of clinical and experimental studies, 746
Book notices, 208
Bones, syphilis of, 415

C

Case of syphilis of the stomach, 740
  of syphilis with bone lesions, 751
  of syphilitic chancre on the scrotum of a patient without penis, 410
  of syphilitic reinfection, 153
Cerebral syphilis, 739, 758
Cerebrospinal fluid, 189, 191, 193, 194
Chancre in the axilla, 560
Chancre of the lip, 563
  syphilitic, 43, 187, 188, 200, 410, 413
Changes in reaction accompanying the precipitation of colloidal gold by spinal fluid, 193
Clinic, venereal disease, 56
Clinical aspect of the initial lesion of syphilis in the male, 187
  and biochemical study of neurosyphilis, 287, 629
  experience with Kolmer complement fixation test for syphilis, 756
  value of the Kolmer complement fixation test for syphilis, 195
Colloid flocculation test for syphilis, 196
Colloidal benzoin reaction in the cerebrospinal fluid, 771
  gold reaction, 193
  gold test of the spinal fluid, 747
  reaction on the cerebrospinal fluid, 189
Comparison of the colloid flocculation test with the Wassermann reaction, 196
  of the colloid flocculation test (Dreyer-Ward Technic) with the Wassermann reaction for the diagnosis of syphilitic infection, 772

Comparison—Cont'd
  of the formaldehyde-gel reaction with the Wassermann reaction, 190
  of the Sigma and Wassermann reactions, 772
  of the Wassermann reaction with the Sachs-Georgi reaction and with the Sigma reaction of Dreyer and Ward, 757
  of the Wassermann test with the Kahn flocculation test in 1,000 cases, 748
Comparative study of Kahn and Wassermann reactions for syphilis, 769
  study of three colloidal reactions on the cerebrospinal fluid, 189
  value of Kolmer's new antigen in the routine Wassermann test, 612
Concerning the specificity of cholesterinized antigens in the serologic diagnosis of syphilis, 755
Congenital syphilis (*See* Hereditary syphilis.)
    of the nervous system, 742
    and the eruption of the first teeth, 185
Controlled prostitution in Coblenz, Germany, 713

D

Deafness, syphilis as a factor in, 203
Delayed congenital syphilis, 204
Diabetes, Wassermann reaction in, 679
Diagnosis and treatment of syphilis, 752
  and treatment of syphilis of the nervous system, 617
  of late, hereditary syphilis and lupus-otorhino-laryngology, 202
  of neurosyphilis, 202
  of syphilitic aortitis, 767

E

Ear, syphilis of, 415
Early diagnosis of syphilis, 754
Effect of antisyphilitic treatment on the kidney, 781
  "Arsenic-fastness" of Trypanosoma-Equiperdum on the ratios between the parasiticidal values of arsphenamine, 736
Effect—Cont'd
  arsphenamine treatment on cardiovascular syphilis in negroes, 767
  mercury inhalations upon the animal organism, 1
  time between obtaining spinal fluid and making a cell count, 191
Elimination of arsenic in the urine after intravenous injection of arsphenamine, 205
Endocarditis as a sequel to syphilitic valve defect, 184
Epoch-making contributions to the study of syphilis, 726
Erythema multiforme caused by arsenic. Report of a case, 778
Excretion of spirochaeta pallida through the kidneys, 184
Experience with the Kolmer quantitative complement-fixation test for syphilis, 770
Experimental studies with mercurials in experimental syphilis, with a brief note on their clinical application especially as to Flumerin, 759
Extragenital chancres, 766
Euglobin group and their relationship to the Wassermann reaction, 191

F

Formalin test for syphilis, 189
Formaldehyde-gel reaction, 190
Frambesiform syphilis, 754
Fundamental principle of the Wassermann reaction, 699

G

Gastric crises of tabes, 186
Gastric and intestinal syphilis; report of a case; clinical course and morbid pathology, 648
Gastric syphilis; a report of two cases proved anatomically, 740
General paresis. What it is and its therapeutic possibilities, 763
Genital chancre, 43
Granuloma inguinale, 186

H

Headache, syphilitic, 416
Heart and syphilis, 184
Hecht-Weinberg-Gradwohl test, 199
Hemianopia as the sole clinical feature in untreated secondary syphilis, 665

Hereditary syphilis, 202, 204, 413, 415, 748

I

Inability of serum with a high cholesterol content to increase the strength of the Wassermann reaction, 756
Incidence of syphilis in hypothyroidism and myxedema in children, 414
  of the Wassermann reaction in a large child-caring institution, 198
Influence of saturation on properties of antigen in the Wassermann test, 772
Inhalations, mercurial effects of, 1, 145
Intensive treatment of early syphilis, 750
Intestines, syphilis of, 648
Insane, syphilis in hospitals for, 183
Interpretation of the Wassermann reaction, 194

J

Jaundice, due to salvarsan, 206
  in syphilitic persons receiving arsenical preparations, 760

K

Kahn precipitation test for syphilis, 389, 687, 743, 768
  test for syphilis in the Public Health Laboratory, 775
Kidneys, excretion of spirochaeta pallida through, 184
Kolmer's complement fixation test for syphilis, 195
  modification of the Wassermann reaction, 770
  new antigen, comparative value of, 612

L

Lange test, 193
Late results in the treatment of syphilis, 736
Lichen Planus eruption after arsphenamin, 780
Lip, chancre of, 563
''Local'' Wassermann reaction: A new diagnostic aid in primary syphilis, 754
Locomotor ataxia (*See* tabes dorsalis)
Luetin test in latent syphilis, 196
Lumbar puncture and prevention of complications, 202
  in the routine treatment of syphilis, 761
Lung, syphilis of, 414

M

Marked atrophy in early tabes, 775
Mental deficiency and syphilis, 203
Modification in the routine treatment of syphilis, 781
Mouth, syphilis of, 413
Mercurosal, 204
  in the treatment of syphilis, 777
Mercury inhalations, effects of, 1, 145
  therapy of syphilis, 145
  therapy of syphilis—shall it be condemned? 326
Mercury versus arsphenamine in the treatment of syphilis, iv, 347

N

Neurorecurrences following treatment with arsphenamine, 205
Neurosyphilis, 185, 186, 197, 201, 202, 203, 287, 617, 629, 663, 665, 720, 758
Neurosyphilis among the Chinese, 412
Neurosyphilis in the aged, 737
Nonspecific cross-fixation of complement with Wassermann and tuberculosis antigens, 193

O

Observations on the colloidal gold reaction in neurosyphilis, 769
  on Kahn precipitation reaction for syphilis, 389
  on the diagnosis of neurosyphilis, 202
  on the Kahn precipitation reaction for syphilis, 687
  on the precipitation reaction for syphilis, 755
  on the treatment of syphilis in pregnancy, 207
  on ten cases of delayed congenital syphilis, 204
Original Sachs-Georgi reaction in the tropics, 192

P

Paralysis of the seventh cranial nerve in early constitutional syphilis, 663
Paresis with negative spinal fluid, 323
Pathogenesis of mercurial stomatitis, 760
Pathological changes in the kidney in congenital syphilis, 741
Plea for the early diagnosis and treatment of cerebrospinal syphilis, 201
Pontobulbar crisis associated with sialorrhoea in syphilis of the nervous system, 764
Positive Wassermann test in a fatal case of estivo-autumnal malaria, 757
Postarsphenamine dermatitis, contributory factors in, 779
Practical observations on syphilis, 83, 417
Preataxia gastric crises of tabes, 186
Precipitation reaction for syphilis, 189, 195, 196, 200
Precipitation test of the arachnoid fluid, 191
  for syphilis of concentrated arachnoid fluid and serum, 744
Pregnancy, Wassermann reaction in, 155
  treatment of syphilis in, 207
Preliminary report of mercurosal, 204
Preservation of complement for Wassermann test, 194
Prevention of syphilis of the central nervous system, 720
Problem of the syphilitic child, 751

Q

Quantitative precipitation reaction for syphilis, 189, 196, 200
  studies with arsphenamine, ii, distribution and excretion after intravenous injection, 746
  studies in syphilis from a clinical and biological point of view, 765
  studies in syphilis from a clinical and biological point of view, iii, arsenical content in scales, blood, and urine in arsenical and nonarsenical eruptions, 209

Quantitative—Cont'd
  studies in syphilis from a clinical and biological point of view, iv, arsenic content in the blood at various intervals after intravenous injections of salvarsan, 225
  studies in syphilis from a clinical and biological point of view, v, arsenic content of the blood and spinal fluid after neosalvarsan in the Swift-Ellis method of treatment, 444
  studies in syphilis from a clinical and biological point of view, vi, arsenic content of the spinal fluid after salvarsan in the Swift-Ellis method of treatment, 478
  studies in syphilis from a clinical and biological point of view, vii, arsenic content of the spinal fluid after salvarsan and drainage, 513
  studies with arsphenamine, 761
  studies with arsphenamine, ii, distribution and excretion after intravenous injection, 746

R

Rapid precipitation phase of the Kahn test for syphilis, 745
Reactions following arsenobenzene administration and their treatment, 160
  in the treatment of syphilis and their probable significance, 761
  the intravenous administration of arsenobenzene compounds, 778
Recent studies on spirochetes in general paralysis, 768
Recognition of congenital syphilitic inflammation of the long bones, 415
Reinfection in syphilis, 766
Relation between syphilis and diabetes mellitus, 765
  of syphilis to diagnosis and surgery, 186
Relative value of Sachs-Georgi and Wassermann reactions in diagnosis of syphilis, 774
Reliability of the Sachs-Georgi test for syphilis, 773
Remarks on visceral syphilis, 671
Reinfection, syphilitic, 153

Report of a case of nodular disseminated nonulcerative syphilide, 415
Results in the treatment of Wassermann-fast syphilis by intravenous mercuric chlorid, 777

S

Sachs-Georgi reaction, 192
Salvarsan jaundice, 206
Serologic changes in neurosyphilitic patients during a period of nontreatment, 197
  studies on the exudate of syphilitic chancre, 188
Sigma reaction for syphilis, 196
Silver arsphenamine, in the treatment of syphilis, 206
Silver therapy, argyria and its relation to, 125
Simple quantitative precipitation reaction for syphilis, 189, 196, 200
Sodium thiosulphate in the treatment of postarsphenamine dermatitis, 608
Specialized favoid scalp condition peculiar to the syphilitic native of South Africa, 185
Specific sore throat which passed as an ordinary pharyngitis and tonsillitis, treatment administered for same, with no relief, 767
Specificity of cholesterinized antigens in the serologic diagnosis of syphilis, 770
Spinal and cistern puncture, with lavage, following apoplectiform attack in paresis, 782
Spinal drainage following intravenous arsphenamine, 205
Spinal fluid examination, value of, 193
Spirochaeta pallida, excretion of, through the kidneys, 181
Spirochetes, staining of, 188
Staining of spirochetes, cover glass smears, 188
Standard of cure in syphilis, 206
Standardization and preservation of complement serum for Wassermann test, 194
Status of lumbar puncture and prevention of complications, 202
  of the negative Wassermann reaction, 773
Stomach, syphilis of, 648
Studies in asymptomatic neurosyphilis, 201
  in familial neurosyphilis, 750
  in syphilis, 412
  on blood cholesterol in syphilis, 774
  of cerebrospinal fluid with an acetic anhydride-sulphuric acid test, 764
  of the Formol and Wassermann reactions, 773
  of the influence of pregnancy in syphilis, 751
  of syphilitic serum reactions, 198
Study of serum flocculation reactions in syphilis with special reference to the Meinicke-Sachs-Georgi, Kahn and Vernes reaction, 742
Sulfarsenol in the treatment of syphilis, 318, 778
Surgery, relation of syphilis to, 186
Syphilis among the insane, further observations, 748
  and marriage, 751
  and mental deficiency, 203
  as a factor in deafness, 203
  as we see it among the natives of Bechuanaland today, 569
  department of the in-patient hospital; its personnel, organization and equipment, 377
  in children, 766
  in general practice, 186, 766
  in hospitals for the insane, 183
  is it curable and can it be eradicated? 203
  of the adrenals, 72
  of the internal ear, 416
  of the lung, 414
  of the mouth, 413
  of the orbit, 742
  of the stomach, 740
  of the testicle confined to the epididymis, 414
  of the uterus, 413
  of the uterus and adnexa, 738
  transmitted to the third generation, 413
Syphilitic backache, 415
  genital chancre, 43
  headache, 416
  macular atrophy, 753
  osteochondritis, 748

Syringomyelia and syphilis of the central nervous system with report of a case of tabes with a syringomyelia syndrome, 759

T

Tabes dorsalis, 186
Tartrobismuthate, toxicity and trypanocidal activity of, 352
Technic of arsenical preparations in the treatment of syphilis, 206
Teeth and syphilis, 185
Test for cure of syphilis, 776
Testicles, syphilis of, 414
Therapeutic action of bismuth in syphilis, 763
Thyroid and syphilis, 414
Toxicity and trypanocidal activity of tartrobismuthate and its relation to the treatment of syphilis, 352
Transmissibility of syphilis in the latent stage, 183
Treatment of arsphenamine dermatitis and certain other metallic poisonings, 779
  of neurosyphilis at the Manhattan State Hospital, 782
  of neurosyphilis, 781
  of syphilis by bismuth salts, 741
  of syphilis with bismuth, 749
Tuberculosis and syphilis, 415
  complement-fixation in, 193
Tumor formation after injection of mercuric salicylate in vegetable oil, 776

U

Ulcerating granuloma, 186
Unusual Wassermann report in a nonspecific case, 756
Use of sodium thiosulphate in the treatment of postarsphenamine dermatitis exfoliativa; report of a case, 608
Uterus, syphilis of, 413

V

Value of bismuth salts in the treatment of syphilis, 762
  of spinal fluid examination, 193
  of treatment in general paresis, 762
Vernes reaction, 190
Venereal disease clinic, 56
  spirochetosis in American rabbits, 187
Visceral syphilis, remarks on, 671

W

Wassermann and flocculation tests, 772
  and Sigma tests, 192
  micro-technic needing only occasional titration of the complement, 755
  reaction, 155, 188, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 612, 699, 771, 775
  reaction as an index of cure, 199
  reaction in diabetes, 679
  reaction in leprosy, 743
  reaction in pregnancy, 155
  test performed with chancre fluid, 200
  variations, 773

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